NICHOLAS KOPELOFF

MAN VERSUS MICROBES

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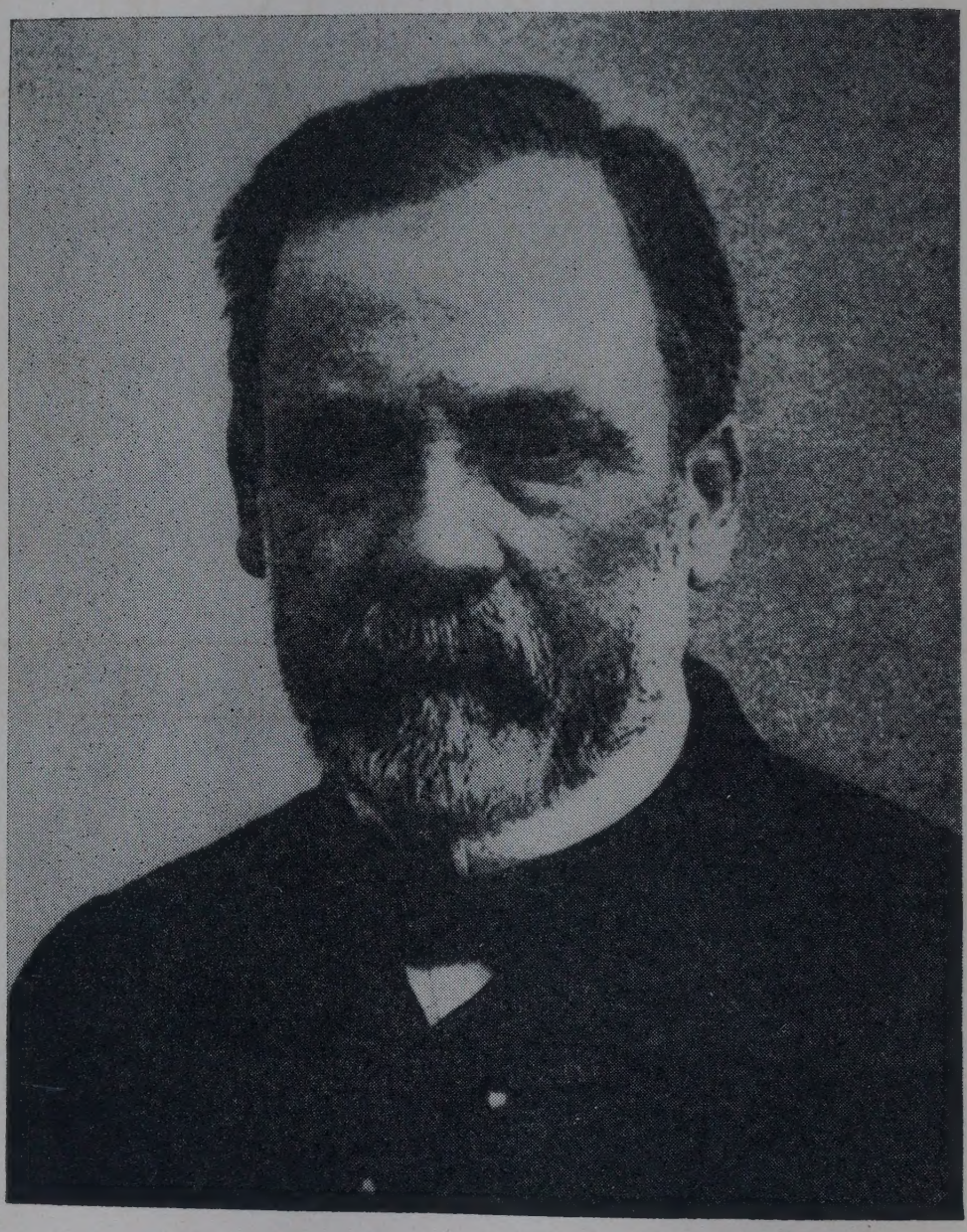
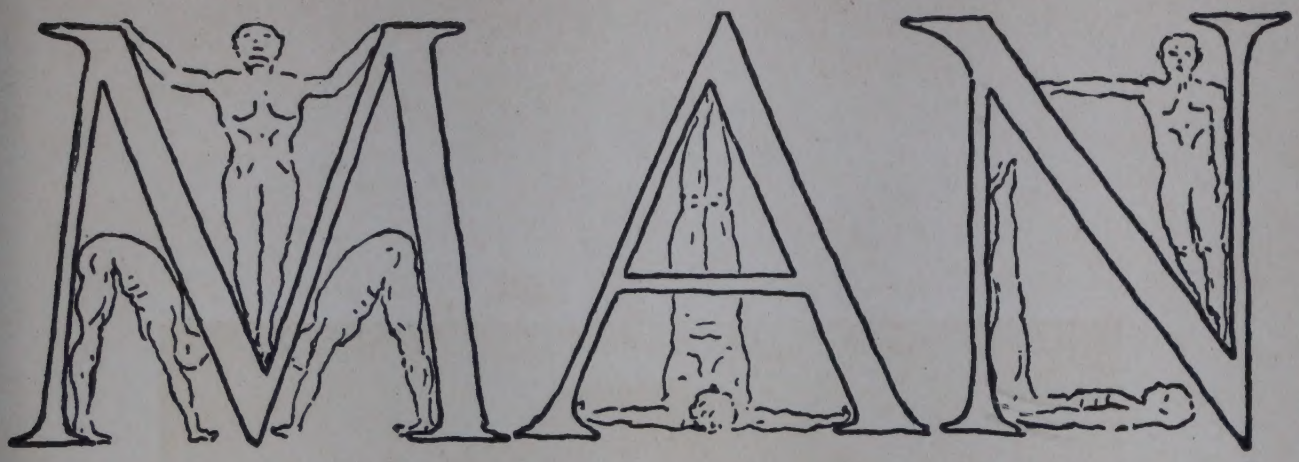


Louis Pasteur. (*After Conn and Conn*)



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MICROBES

BY NICHOLAS KOPELOFF

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FOR

HELEN VERA

Some Day

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Some Day

"The progress of science implies not only the accumulation of knowledge, but its organization, its unification, and this involves the periodic invention of new syntheses, coordinating existing knowledge, and of new hypotheses, which give us methods of approaching the unknown. Science is essentially a system, but instead of being, as it was for the schoolmen, a closed system, it is never closed, but always subject to revision or even to complete discard. The true scientist considers his theories not as perfect and permanent, but as essentially incomplete and precarious; he is ever ready to abandon any part or the whole of them, should new experimental facts make it necessary. There are scientific methods; there are no scientific dogmas; there is no scientific orthodoxy." — GEORGE SARTON: INTRODUCTION TO THE HISTORY OF SCIENCE.

PREFACE

"A man is only what his microbes make him," says R. T. Morris. And, it might be added, their numbers are as appalling as are the tomes dealing with them. There are text-books for the bacteriologist, for the protozoologist, for the mycologist, and for the microbiologist. There are, further, bacteriologic texts for physicians, dentists, laboratory diagnosticians, college students, and even for nurses. But there is no comprehensive volume on microbes for the intelligent layman. This is an aspect of the human adventure too long neglected.

Interest in microbes and their manifold activities has grown apace. Bacteriologic discoveries or near discoveries have unquestioned news-value. For lack of accurate knowledge such matters are likely to prove, at the best, mere romance rather than scientific realism. Nor are the facts inaccessible, for the inquiring reader may turn to any number of standard bacteriologic text-books of indubitable value, which have served as a basis for the present volume. But a standard text is forbidding to a layman, no matter how interestingly it is written.

This book is therefore offered as perhaps a new species. Its roots, if you will, gather sustenance from the deep fertility of other minds. It is to be hoped that its fruits will prove at once palatable and nourishing.

The temptation to dramatize the great discoveries in bacteriology is well-nigh irresistible. Yet to yield to such temptation involves assumptions which belong more to the realm of fiction than of fact. The present intention, therefore, is to include verifiable facts alone.

Obviously, some selection of the available material must be exercised, else the volume would expand to a size which would defeat its own ends. While the chief emphasis in any consideration of microbes naturally falls upon their disease-producing powers, nevertheless special attention may be directed to those chapters dealing with the microbes of non-medical interest which have been harnessed by man, to his everlasting benefit, in agriculture and industry.

If this book has any particular merit it lies in the fact that it is a compact yet comprehensive survey of all the important microbes — that is, bacteria, moulds, yeasts, and protozoa — not only in medicine, but in agriculture and industry as well. The aim has been to present all the information the layman might desire upon encountering some bacteriologic topic of the day, in his newspaper, magazine, book, or after-dinner conversation.

To this end I have been helped by much friendly counsel. I owe particular thanks to H. L. Mencken, editor of the AMERICAN MERCURY, *Drs. Charles O. Fiertz, Bertram D. Lewin, and Leo M. Davidoff for their invaluable constructive criticism, and to Professor Morton C. Kahn of Cornell University for his kindness in going over the manuscript.*

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MAN VERSUS MICROBES

Chapter I

THE STORY OF BACTERIOLOGY

Man is master of the world he lives in. Unlike his forbears, he laughs at wind and weather. Wild animals have become his household pets, and noxious plants have been transformed into toothsome delicacies. The earth's crust is moulded to suit his every whim — levelled here, scraping the sky there. He hurtles across continents, telescoping the miles into a breathless panorama which fits snugly within the window of a flying train or the windshield of a racing automobile. He ploughs the ocean with steel tempered to hold a ballroom and all the appointments of a modern hotel. He wings the air in cabins *de luxe*.

But on land or sea or in the air man the master is surrounded by an unseen foe — a deadly, innumerable foe, ever mobilized for battle, ever active, giving man no respite, awake or asleep. Speed as he may, the victim never escapes, for so subtle is the foe that man himself is forced to act the unwilling accomplice and the betrayer of his own kind.

In the daily round of human life the unseen host finds limitless opportunities for attack. The final outcome is a long list of individual casualties. How is one to know that from a towel an intensive inflammation of the eyes and blindness may follow; that an inoffensive pimple when squeezed may lead to blood-poisoning, high fever, and death; that the consumption of raw unwashed vegetables may cause severe diarrhœa accompanied by fever; that a neighbour's sneeze may result in swollen tonsils and a siege of fever, followed by heart-disease; that irregular sexual intercourse may lead to general paralysis which numbs the body and disorientates the mind? What insidious enemy is this which spares no living thing, which makes of every living moment an imminent peril? How does one fight an unseen foe?

It is the purpose of this book to make a complete reconnaissance of our ever-present enemies the microbes. What have we

learned of their armament, of their methods of attack? How may we best repulse them? What are our chances of ultimate success? From the dawn of human life to the seventeenth century man's ignorance of microbes was complete. And ignorance was any-

FIGURE 1

Van Leeuwenhoek, father of microscopy. (After the "Deutsche Medizinische Wochenschrift.")

thing but bliss. Countless generations succumbed before there came a beam strong enough to penetrate the unknown.

The story of bacteriology is at once a romance and a realistic tale of supreme human achievement. The illustrious names which mark its pages have become familiar; the memory of the many laboratory workers who have gone unsung is none the less cherished by those who adjust the microscope and inoculate the guinea-pig. From van Leeuwenhoek to Noguchi, research in bac-

teriology has been as the development from the first rough-hewn cave to the modern sky-scraper. Let us first take an airplane view.

What the bathtub was to Archimedes, and the falling apple to Newton, lenses were to van Leeuwenhoek. (See fig. 1.) Anthony van Leeuwenhoek was a common citizen of Delft, a linen-draper

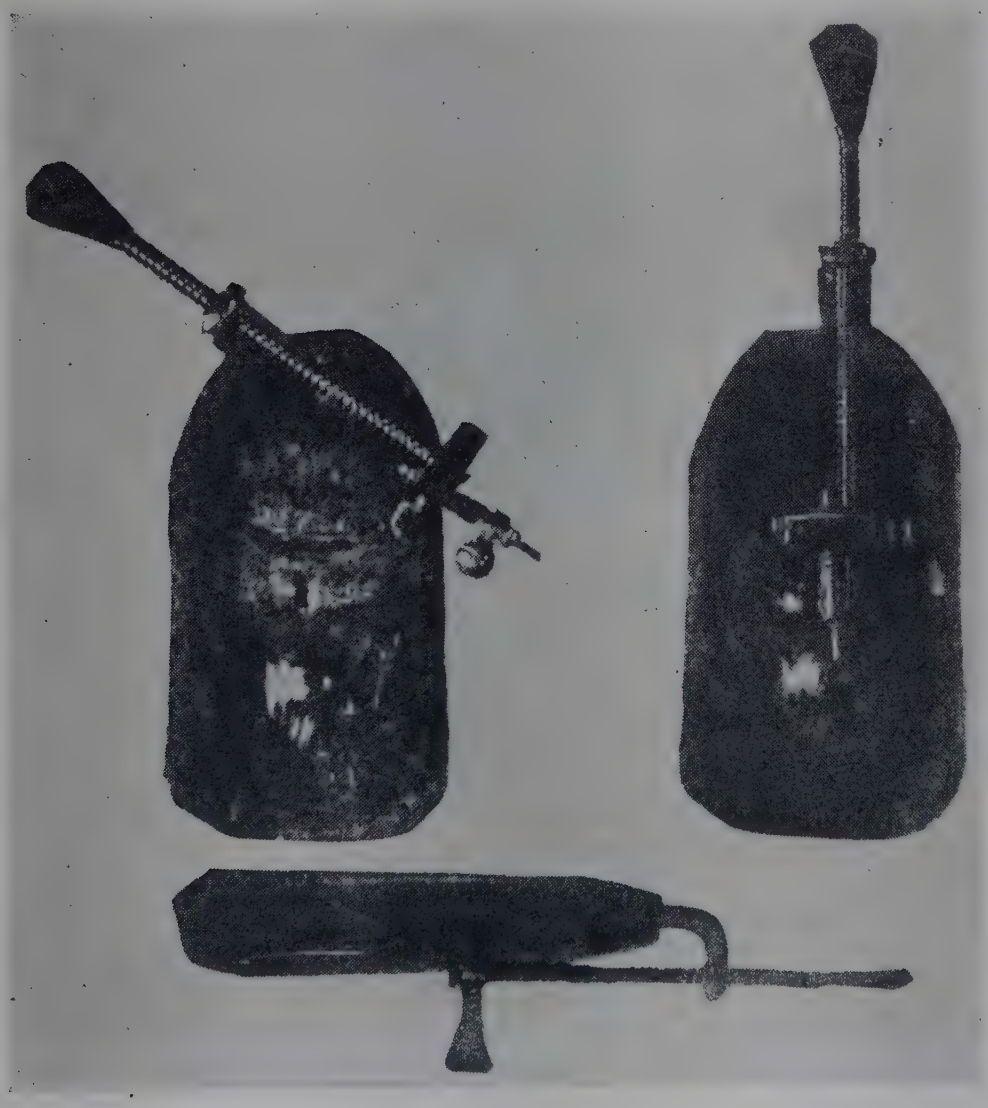


FIGURE 2

Van Leeuwenhoek's microscope. Natural size. From photographs by Professor Nierstrasz, of Utrecht. (After Locy.)

by profession. As a youth he had learned the art of grinding small lenses and polishing them so fine that they were able to magnify greatly whatever object he examined with them. But what was the magnification obtained with a simple lens, however perfect, compared with a combination of lenses? It was this ingenious idea which won for him the title of "father of microscopy." The finest microscopes today, magnifying objects

more than two or even three thousand diameters, are but the logical development of van Leeuwenhoek's simple but effective seventeenth-century device. (See fig. 2.) He set two minute lenses between metal plates and brought into focus a new world. Lilliput was turned into Brobdingnag! Familiar objects assumed gigantic proportions, unknown objects swarmed into sight. Everything went under his lenses for examination: sea-water, spring-water, shreds of vegetable and animal tissue. No matter how diverse the material, it was found to be teeming with animated forms: "tiny animalcules." Their presence was universal in all familiar things, internal as well as external. Rain-water, previously thought to be pure, was literally alive; so, too, the intestines of the chicken, the pigeon, the frog, and even of van Leeuwenhoek himself. No flight of the imagination could picture how densely populated was the invisible world. Van Leeuwenhoek set himself the task of painstakingly describing its inhabitants.

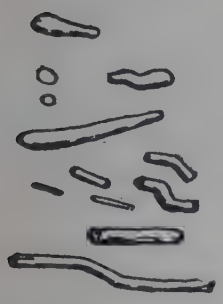


FIGURE 3

Van Leeuwenhoek's drawings of "animalcules." (After Conn and Conn.)

In his letter to the Royal Society of London, dated September 14, 1683, now a classic, are recorded his findings of the preceding eight years, accompanied by drawings of tartar scraped from his teeth: "I saw with great amazement that this material contained many tiny animals which moved about in a most amusing fashion; the largest showed the liveliest and most rapid motion, moving through the water or saliva as a fish of prey darts through the water; they were everywhere, although not in large numbers." He further describes other forms, some "spinning around like tops; others, exceedingly tiny, moved so rapidly helter-skelter that they looked like a confused swarm of dancing gnats or flies." (See fig. 3.)

From the discovery of "animalcules" stems the imposing science of bacteriology. It seems incredible that within the short space of two hundred and fifty years we should not only have learned the causes of so many infectious diseases — diphtheria, typhoid fever, pneumonia, and the like — but have also developed antitoxins, vaccines, and serums for their prevention and treatment. Compare the progress made in the biologic sciences before and after the accumulation of this knowledge! How many centu-

ries before the seventeenth did man suffer and benefit by the presence of living organisms he could not describe! In modern times medicine, industry, and agriculture all lean heavily upon bacteriology. Our daily life is a continuous application of its principles, from the matutinal tooth-brush to the nocturnal prophylaxis.

It might be assumed that, following van Leeuwenhoek's perfection of the microscope and his consequent discovery of bacteria, tremendous advances would speedily have been made. In point of fact, a century elapsed before anything of significance was accomplished. Possibly those who looked through the microscope were too much fascinated by the multiplicity of forms they encountered to do more than wonder. Yet certain similarities must have been evident. Finally O. F. Müller, in 1786, undertook a systematic classification which brought some order into the chaotic knowledge of these microscopic beings. In his own words: "The difficulties involved in the investigation of these microscopic animals are innumerable; their true and sharp definition requires so much time, such keenness of eye and judgment, so much equanimity and patience as scarcely anything else." Fifty years later Ehrenberg succeeded in giving a still more accurate account of bacteria, differentiated clearly the spherical, rod, and spiral forms. Some of the terms he used, such as "bacterium" and "spirillum," have endured to the present day.

But it was one thing to describe bacteria, another to explain whence they came and what they did. The traditional belief was that living things were generated spontaneously. Aristotle believed that eels could originate from mud. Van Helmont, in the sixteenth century, gave a formula for the creation of mice: soiled cloth and some grain or fragments of cheese. The putrefaction of meats and other products was to be expected in the natural course of events; but the microscope examination of decaying objects raised a perplexing problem, for myriads of bacteria could be discerned. Where did they originate? Did those minute living organisms come from the air or were they generated spontaneously in liquids? Controversy over this point raged for many years. Experiments ingenious and interesting were performed. If one faces the problem naïvely, it is truly a difficult one to solve. If you were taxed with it, what conclusive

demonstration could you devise to prove that microbes did not originate spontaneously?

Probably the most obvious approach would be to place meat broth or some other test liquid in a bottle and cork it tightly to prevent the access of air which might carry microbes. But within twenty-four hours the broth would swarm with microscopic organisms. Evidently sterner precautions must be taken. How kill

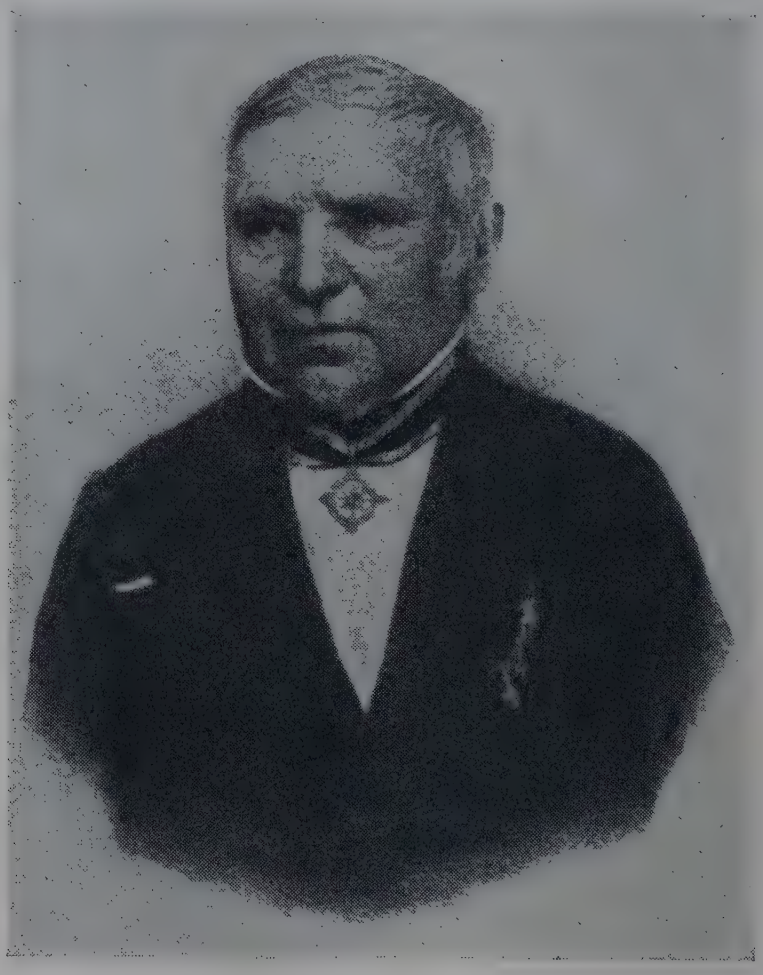


FIGURE 4

Ehrenberg. (*After Locy.*)

the microbes which are in the broth itself? Electrocution was centuries away from van Leeuwenhoek's time. Fire offered real possibilities for destruction. Why not cork a flask tightly and heat it? The reasoning is sound — but what of the results? Needham, a Roman Catholic priest, actually performed this experiment in 1749 and found that broth in heated, cork-stoppered flasks occasionally remained clear, but more often became turbid in a few days, this turbidity being due, on microscopic examination, to the presence of enormous numbers of living microbes.

Was he justified in concluding that these must have been spontaneously generated?

Not according to the Abbé Spallanzani, who brought a singularly critical faculty to bear upon the details of Needham's experiments. What a commentary on the present Fundamentalist battle against evolution, that in the eighteenth century church-

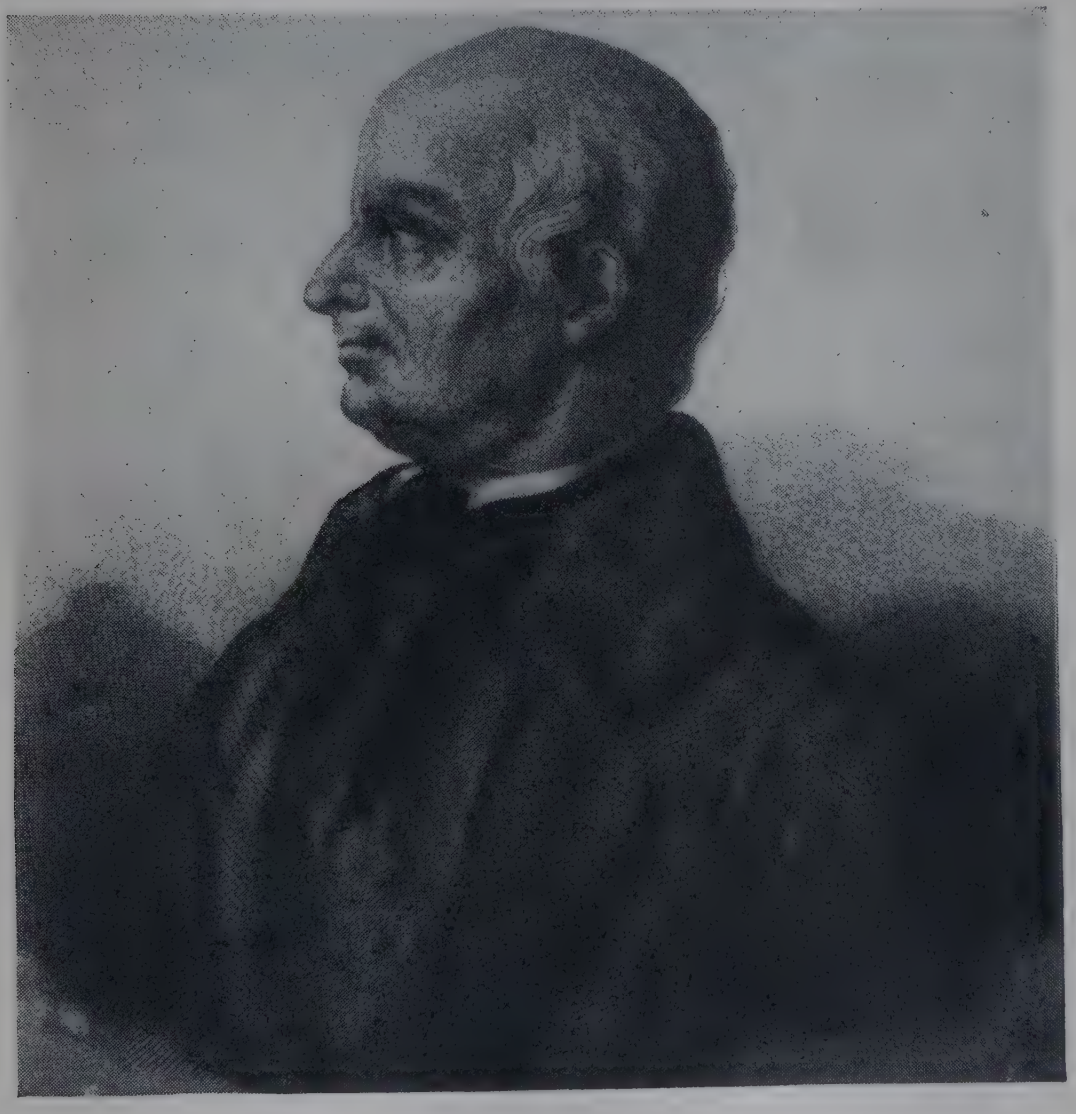


FIGURE 5

Lazzaro Spallanzani. (*After Locy.*)

men were performing crucial scientific experiments! Spallanzani saw several possibilities for error; for instance, was it not possible that Needham had not sealed his flasks perfectly or that they had cracks which permitted micro-organisms to enter? Again, was the temperature of the hot ashes used by Needham to heat his flasks sufficient to kill all the living organisms or prevent them from reproducing? First Spallanzani demonstrated that bacteria invariably develop in *unheated* broth even though the

flasks were *hermetically* sealed and free from cracks. But there still remained the problem of killing the bacteria originally present in the contents of the flask. Let him speak: "I placed nineteen different infusions in as many hermetically sealed flasks and boiled them in water for one hour. When I examined the flasks at the proper time, there was no sign of spontaneous movement, which enabled me to exclude any presence of living creatures in the infusions, no matter how much I searched for them later with the microscope. Many subsequent experiments gave the same results. If by gentle pressure one made several cracks in the flasks after boiling, so that some air might enter, tiny animals could be found." Spallanzani concluded from these fundamental experiments that the "tiny animals" required air.

Needham was obviously worsted, but later experimenters objected to Spallanzani's procedure, chiefly on two grounds. To begin with, the flasks may not have contained sufficient air to support growth. In other words, hermetically sealing a vessel necessarily limited the amount of air essential for the microscropic living organisms. Perhaps they required more air than Spallanzani allowed them. The other objection reflected upon Spallanzani's practice of boiling the flasks. Did Spallanzani know what alteration might be produced in the composition of the air by boiling it? Possibly it became unfit for life, much as boiling an egg coagulates the proteins, thereby making them less digestible.

Schulze in 1836 met the first criticism, but failed to dispose of the second. In order to allow air to enter a previously boiled flask of broth without adding living organisms he conceived the idea of first passing the air through concentrated sulphuric acid. This killed all living forms, and the broth remained free from growth. Similarly, a year later, Schwann passed air through a red-hot tube into flasks of previously heated broth. They too remained free from growth. But critics asserted that concentrated acid or red heat might well have changed the composition of the air introduced. How, then, add untreated air?

The problem resolved itself into a search for some material porous enough to allow air to enter a flask, but dense enough to keep out microbes. Cotton proved to be ideal for this purpose. To Schröder and von Dusch belongs the credit for this noteworthy solution to a perplexing problem. In 1854 they plugged their

heated flasks with cotton. This permitted the passage of air, but filtered out the dust particles and organisms living in the air. To this day cotton-plugged glassware is to the bacteriological laboratory what the air tube is to the deep-sea diver.

Finally, Pasteur and Hoffman (1860), independently, cut the Gordian knot by applying the Newtonian law of gravity. They reasoned that microbes, being heavier than air, would fall and not rise in an enclosed space. By the simple expedient of drawing out the neck of a flask into an inverted horizontal S shape they were able to prevent bacterial growth in their flasks. Air entered the upturned end of the tube, but dust particles, together with bacteria, settled in the bend and could not rise against gravity into the long arm of the curved tube. The broth remained unspoiled. (See fig. 6.)

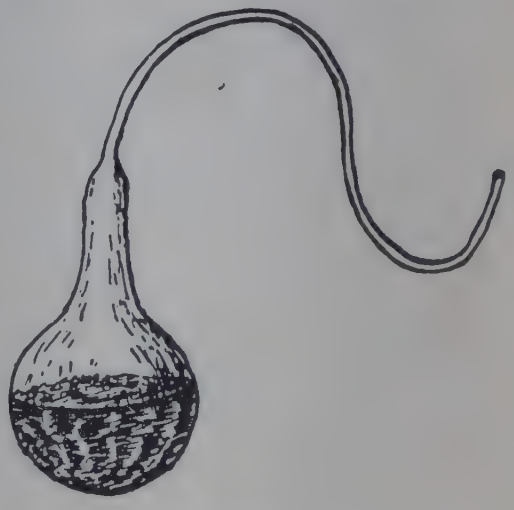


FIGURE 6

Pasteur's culture flask. (After Löffler in Conn and Conn.)

It followed that the more dust, the more contaminated (by bacteria) the air. Pasteur confirmed this generalization by direct observations. He found that heated flasks opened in the dust-laden atmosphere of Paris became speedily contaminated with bacterial growth, while on a hill-side near his father's tannery, only eight of twenty flasks showed growth. "Pasteur went on to Salins and climbed Mount Poupet, 850 metres above the sea-level. Out of twenty vessels opened, only five were altered. Pasteur would have liked to charter a balloon in order to prove that the higher you go, the fewer germs you find, and that certain zones are so absolutely pure as to contain none at all. It was easier to go into the Alps." Thus does Vallery-Radot in his classic *Life of Pasteur* describe the zeal which was rewarded by finding that only one flask in twenty showed any sign of bacterial invasion at the glacier above Chamonix.

This dealt the death-blow to the theory of spontaneous generation. It was strengthened by Tyndall's demonstration, in 1876, that flasks of sterilized material might remain uncontaminated even when left open in a small chamber from which dust particles

had been excluded to such an extent that none could be seen in the path of a bright ray of light. Prior to this, in 1871, Cohn had successfully explained why, in experiments such as Needham's, bacteria had proved so resistive to heat. Many of them go into a spore or resting stage when confronted by adverse conditions,

FIGURE 7
Ferdinand Cohn. (*After Locy.*)

such as excessive heat or cold, much as a snail withdraws into the protection of its shell.

The spore with its resistive thickened envelope represents a quiescent stage in the life of a bacterial species. When conditions are again favourable, each spore may germinate into a bacterium, and thus propagation continues. Needham killed many living bacteria, possibly all, when he heated his broth flasks, but he failed to injure the spores which germinated after a few days and this led him unwittingly to believe that spontaneous generation had occurred. Pasteur showed conclusively that microscopic organisms, like larger animals or plants, always have parents like

themselves; a living thing comes from living things, "*omne vivum ex vivo.*"

Whence comes the name "bacteria"? Van Leeuwenhoek called his microscopic discoveries "animalcules." Spallanzani referred to them as "tiny animals." Ferdinand Cohn in 1872 set an enduring fashion when he named them "bacteria." The word comes from the Greek meaning "staff" or "stick." Doubtless he was prompted in his selection by the fact that the microscopic organisms of greatest interest in his day were rod-shaped. Six years later, Sédillot coined "microbe," a far more inclusive term, compounded from the Greek "*μικρός*," meaning "small" and "*βίος*" meaning "life." "Small life" is descriptive, but curiously inaccurate etymologically, for the combination of "*μικρός*" and "*βίος*" in Greek means "shortlived." "Microbes" is what Sédillot called them and microbes they remain, comprising all kinds of micro-organisms — that is to say, bacteria, yeasts, moulds, and protozoa.

The microbial world is densely populated with many different forms. Immediately the question arises as to whether bacteria are plants or animals. The problem is more easily posed than solved. For the present it is enough to say that, in general, one thinks of plants as green, branching, stationary objects, whose seeds are scattered about. Algæ, those floating strands of seaweed, are really the lowest form of plant-life possessing green colouring-matter (chlorophyll).

But there are even lower forms of plant-life — moulds — which do not have this green pigment and which are so small that the individual organisms cannot be seen with the naked eye. Large numbers of them in masses are familiar because their fruiting bodies, corresponding to seeds, have colour. They may be seen in all kinds of mouldy or decaying matter: the green spots on an over-ripe orange or on old cheese, or the black patches on soggy bread. This gives them their name of "moulds" or "fungi." Under the microscope a single mould is a fine branching thread which grows indeterminately, forming dense skeins of threads. At various points fruiting bodies develop which colour the mass. When one observes the green spot on an orange, one sees only the fruiting bodies — one does not see the enormous underlying mass of coiled threads. Not only are moulds unappetizing — for no one

relishes the thought of ingesting skeins of threads — but some are positively dangerous, causing diseases of the mouth and skin.

Closely related to the moulds are the yeasts, the difference between moulds and yeasts being that yeasts, which are also microscopic plants without green pigment (chlorophyll), multiply, not by branching, but by budding, each cell giving rise to a

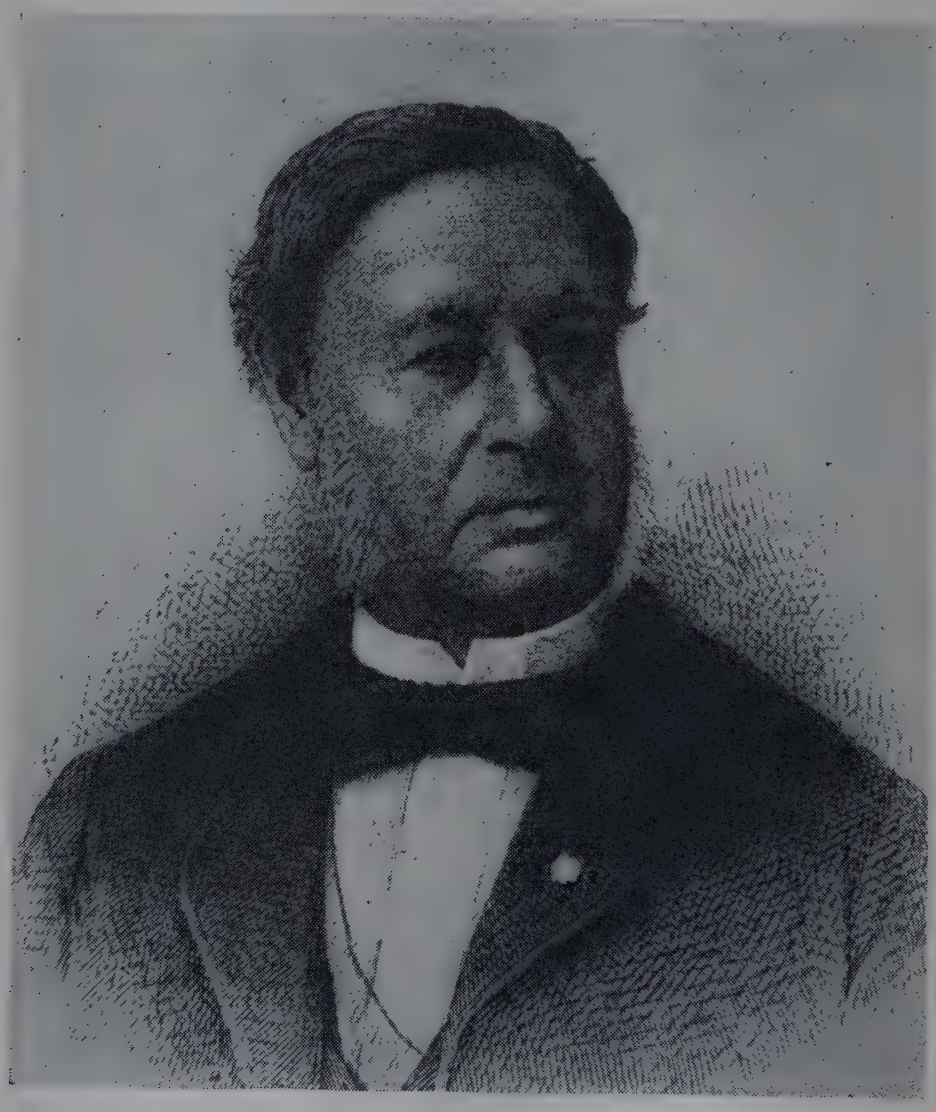


FIGURE 8

Theodor Schwann. (*After Locy.*)

daughter cell which adheres to its parent. Yeast is best known as a compressed square or yeast cake, composed of millions upon millions of yeast cells. But yeasts are to be found in all kinds of fermenting substances — grape juice, syrups — in short, in anything which contains sugar dissolved in water.

On the one hand, therefore, bacteria have much in common with moulds and yeasts, the lowest forms of plant-life; on the other hand they are not far removed from the simplest form of

animal life, the protozoa. Again, the protozoa are microscopic in size, but each cell has a well-defined central structure, called a "nucleus," not to be found in moulds, yeasts, or bacteria. Protozoa thrive in the presence of an abundance of moisture, as in stagnant pools and the like. Protozoa are large enough to devour bacteria, and do so, avidly. Moulds and yeasts have no such cannibalistic tendencies towards their microscopic brethren. The discovery of each of these large microbial groups, the bacteria, moulds, yeasts, and protozoa, has been of great significance to mankind, for, as we shall soon see, each has the capacity to produce disease.

While experimenters quarrelled over the problem of spontaneous generation, the practical-minded Schwann, who had contributed his bit by passing heated air into flasks of broth, turned to more fertile fields. He drew attention to an important group of microbes other than bacteria — namely, the yeasts. Yeasts were described in 1837 by Schwann and also observed independently in the same year by Cagniard-Latour. In the days before bread-making became a standardized industry, every farmer's wife knew that it was yeast which made bread rise. Today yeast is something to be purchased in the drug-store, candy-coated or *au naturel*, for any and every conceivable ailment. Yeasts have been defined by Tanner as "fungi or moulds which cause many changes in food." Schwann discovered that they fermented sugar solutions. Better still, he demonstrated that the alcoholic fermentation of sugars can go forward only in the presence of yeasts, and that the latter grow during the process. To this, many a prematurely popping cork will testify.

But fermentation is not confined to the activities of yeasts, as Pasteur discovered — nor is the end-product always alcohol. Milk, for example, contains sugar, which may be fermented by bacteria to form lactic acid, making sour milk, another pleasant if less stimulating beverage lately reputed to be a panacea for all intestinal ailments, as well as an aid in the prolongation of life. Pasteur showed, however, that if milk is first boiled, natural fermentation produces, instead of lactic acid, another, less palatable acid, butyric, that rancid-butter acid of characteristically unpleasant odour. By using an acetic-acid-producing microbe in cider, Pasteur devised an improved method of making vinegar,

which represents still another type of fermentation. And there are many more. In fact, "fermentation" is a term which may be applied to the breaking down of any sugar or other carbohydrate (a substance containing carbon, hydrogen, and oxygen in definite proportions). It is one of the manifold activities of microbes, and its systematic study has formed a small part of all the knowledge that has gone into the making of a new science.

Pasteur it was who revealed the importance of microbes in nature. "If any one man can be looked upon as the founder of the science of bacteriology, that man is surely Louis Pasteur," says Jordan. His vision enabled him to go far beyond the fundamental demonstration that microbes were not generated spontaneously in putrefying liquids, to a consideration of microbes in all "natural" processes, such as fermentation, putrefaction, and decay. Microbes are to be found in every stage of decomposition, but, as Pasteur showed, their presence is not accidental — it is essential. Microbes cause decomposition by using the original vegetable and animal materials as a source of food and in gaining their livelihood they alter the composition of the original material beyond recognition. The decomposition of animal or vegetable matter is known as "decay" — as when an apple falls to the ground and through the agency of microbes rots away, eventually to form soil. Decomposition in the absence of oxygen, as in the interior of a rotting carcass, is known as "putrefaction," and results in the formation of foul-smelling substances. The decomposition of carbohydrates, as we have already observed, is known as "fermentation." In a word, as Pasteur clearly pointed out, putrefaction, decay, and fermentation are by-products of the activities of microbes in nature. But of what value were these fundamental scientific observations to his practical countrymen?

The "rosy and tawny wines" of the Jura were turning bitter and greasy, so Pasteur was called on, in 1864, in the hope that he might rescue them. Boiling would kill the offending microbe, but what Frenchman with an appreciation of bouquet would drink boiled wine? A brilliant yet simple method proved effective. Heat destroys living microbes. By heating wine for a few moments at a moderately high temperature, 135° Fahrenheit (212° being the boiling-point of water), its keeping quality was assured and its flavour remained unimpaired. This difficult problem ter-

minated, therefore, in the procedure which makes of his name the verb "pasteurize." Pasteur, with his knowledge of microbes, saved the wine industry of France.

The principle of a short preliminary heating is now also universally applied to milk to safeguard it against spoiling. Nor must we fail to give credit to the French confectioner, Appert, who in 1811 applied the same principle to other foodstuffs with conspicuous success. Fruits, vegetables, and liquors were preserved by heating and sealing them in vessels. Today the Frenchman visiting New York eats peas from his native land, the Californian his asparagus from the sun-kissed Pacific slope, and the bachelor husband dines out of the tins his wife bequeathed him. A great packing and canning industry ramifies over the globe — thanks to two Frenchmen who put science to daily use.

Pasteur was of the soil. He knew what vineyards were before he went to the Jura to save the wine industry. But he knew little of that great industry of southern France — silk production. The silkworms were being destroyed by an epidemic disease of unknown origin. It was responsible for widespread poverty and distress. The financial loss alone was estimated at about twenty million dollars. In their extremity the silk-growers prevailed upon Pasteur to come to their aid. It was a perplexing situation, but in his inimitable way, for he possessed the faculty of correlating miscellaneous observations so as to strike at the heart of an unfamiliar problem, he grappled with it for several years. Finally he discovered the microbe which caused the disease called "*pébrine*," and devised remedial measures for its control. This was the first time that a specific microbe had ever been causally related to a disease.

Disease in those days was synonymous with death. It is impossible to conceive the extent of mortality which followed accidental infections, surgical operations, or childbirth. "The prick of a pin is the open door to death," said Velpeau. Men, women, and children writhed in their beds rather than be transferred to germ-ridden hospitals, which to them meant certain death. But a new era was dawning. Lord Lister (see fig. 9) gained world-wide renown as the first to apply antiseptic principles to surgery, with a consequent saving of human life. To Pasteur, whose ideas had

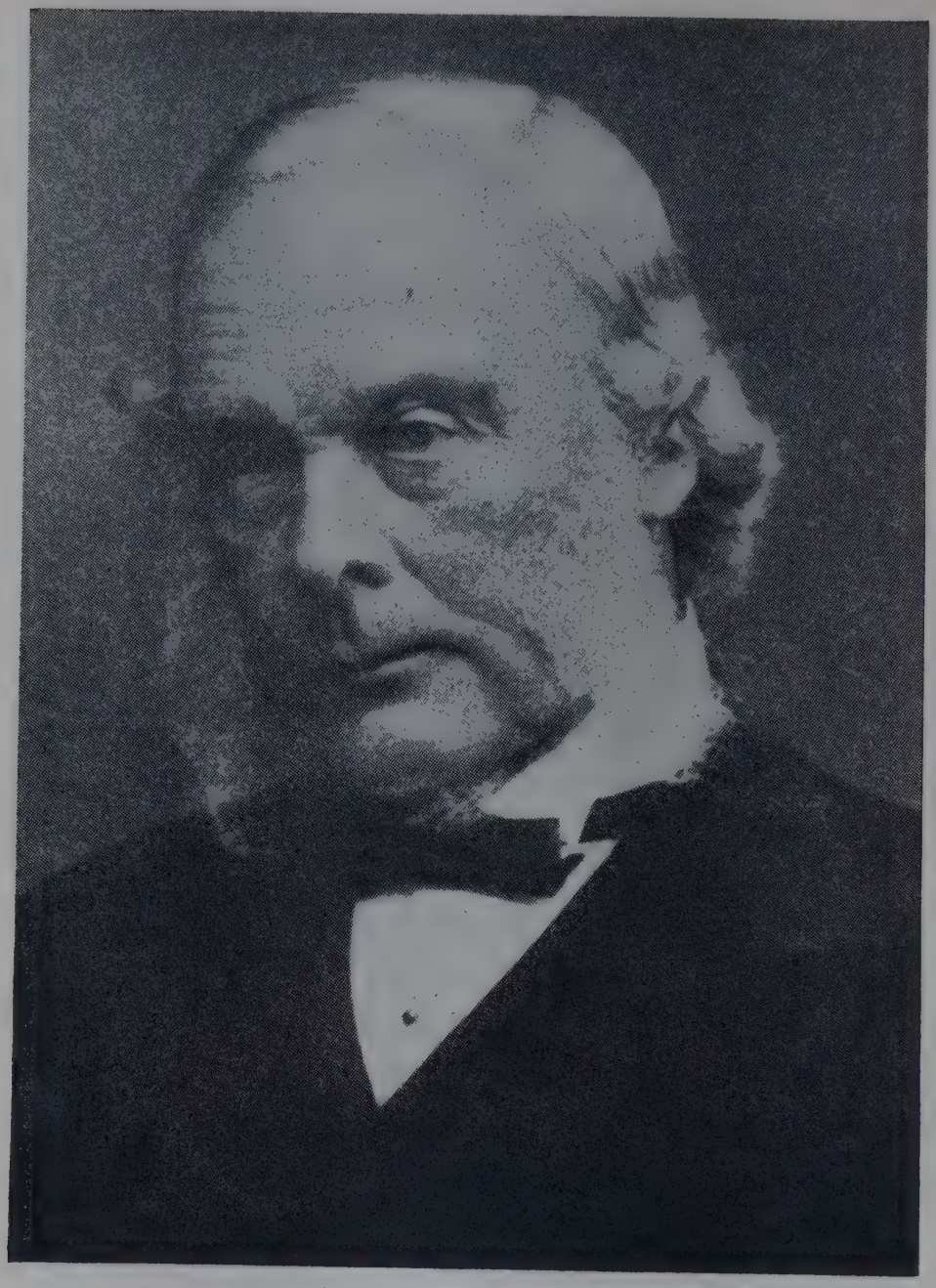


FIGURE 9

Lister, the founder of antiseptic surgery. (Courtesy of New York Academy of Medicine.)

inspired him, he thus modestly pays tribute: "Truly, there does not exist in the entire world any individual to whom the medical sciences owe more than they do to you; your researches on fermentation have thrown a powerful beam, which has lightened the baleful darkness of surgery and has transformed the treatment of wounds from a matter of uncertain and too often disastrous empiricism into a scientific art of sure beneficence. Thanks to you, surgery has undergone a complete revolution, which has deprived it of its terrors and has extended almost without limit its efficacious power."

The long list of Pasteur's contributions are too numerous for more than brief mention. In 1877 he demonstrated successfully that a bacillus which he was able to isolate in pure culture was the cause of anthrax, the dreaded disease of the tanneries, which attacks cattle and man alike. Soon after, he discovered the cause of the diseases known as chicken cholera and swine-fever. Finally he turned his attention to hydrophobia or rabies. The bite of a mad dog meant a horrible death. The disease was not one with which to trifle. Experimentally, Pasteur succeeded in infecting rabbits with the virus of rabies. The disease process appeared to be localized in the brain and spinal cord. Consequently he removed the spinal cords of these rabbits and dried them slowly, causing the infectious agent to lose its virulence. Gradually increasing doses of the virus which actually causes the disease, this virus first having been weakened by drying, are injected into the bitten patient. The resistance of the rabies victim is thus gradually built up until he can withstand a strong dose of virulent virus — after which the virus of the mad dog is nothing more than another dose. But why, one might ask, does not the victim die of the virus, since he has already been bitten? Fortunately it takes a month or two, sometimes longer, for the virus introduced by the bite of a mad dog to become effective enough to cause the paralysis which results in hideous death. An analogy may be found in measles, where it takes about two weeks for the rash to break out after infection has taken place. In rabies the month or two which represents the period of incubation may be utilized for building up, in the manner described, a special resistance to the virus. Over fifty thousand individuals have been treated within ten years with an average mortality of one per hundred. From pasteurization to the Pasteur treatment of rabies is a far cry. It is amazing that one man could accomplish so much for his fellows and for posterity. In gratitude for his discovery of a successful treatment of rabies the Pasteur Institute was erected in Paris by popular subscription. Today it stands in the van of bacteriologic progress — a tribute to its inspiring genius.

The master mind of Pasteur has dominated bacteriology from his day to ours. His aphorism "It is characteristic of science and progress that they continually open new fields to our vision" is indicative of his own life-work. Each advance in bacteriology is a

monument to his achievement. Within and without his profession homage has been paid him. Pasteur belongs not to the bacteriologists, not to the biographers, not even to adoring France: he belongs to humanity for all time.

Bacteriology has become so much an integral part of medical science that it is difficult to think back to the time when the

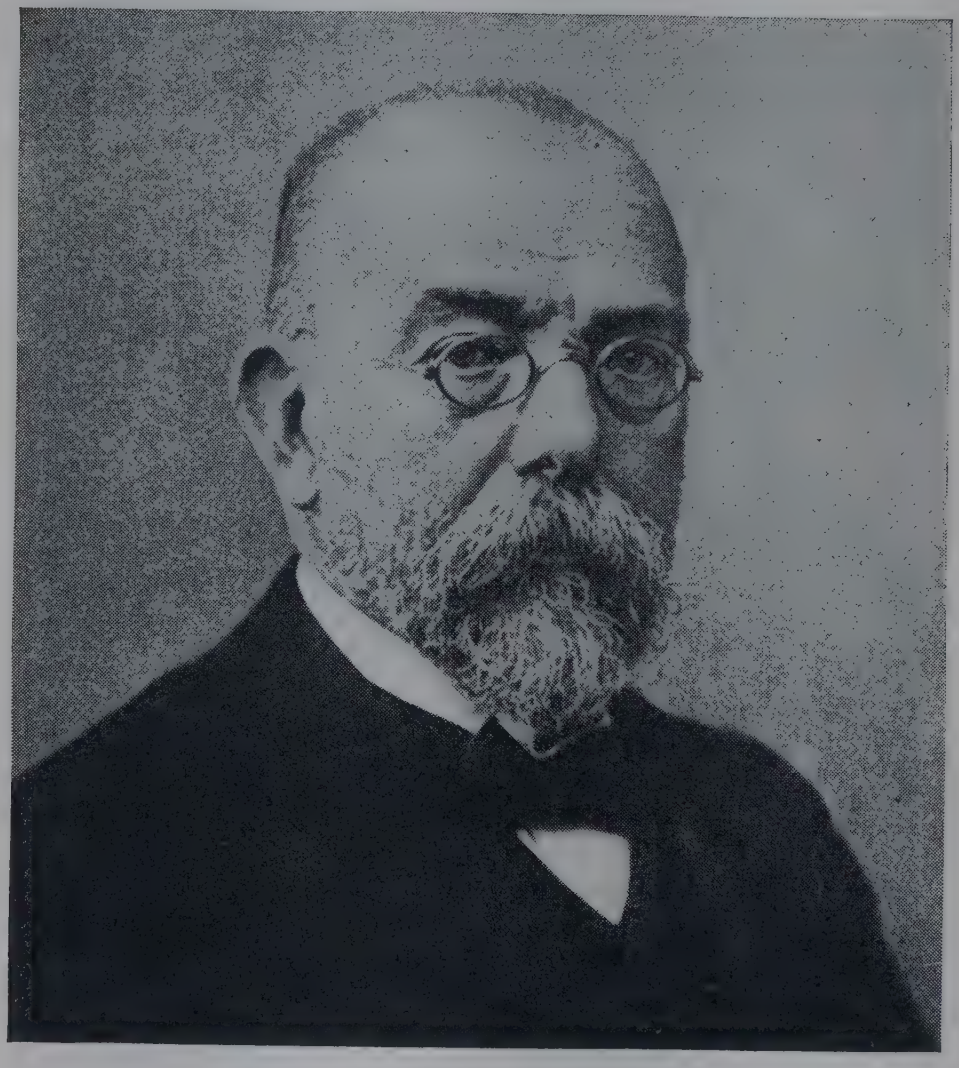


FIGURE 10

Koch, who made of bacteriology a science. (Courtesy of New York Academy of Medicine.)

chief interest in microbes was concerned with their rôle in nature. Through his studies with the silkworm Pasteur showed for the first time that a specific microbe caused a specific disease of moths. From this it was logical to suppose that human disease might likewise be caused by microbes. Plenciz in 1762, a century before Pasteur's discoveries, made just such a suggestion. Without offering any experimental evidence he asserted that every human disease was caused by a specific agent which multiplied

extensively in the patient and that such microscopic agents might be disseminated through excreta in such a way as to disease other human beings. One can only marvel at an imagination which proved so truly prophetic. But it remained for Pasteur to blaze the trail.

There is but one who can rank with Pasteur — Robert Koch, who made of bacteriology an exact science. (See fig. 10.) Pasteur had been trained in science — he was originally a chemist and had made his mark in chemical research before turning to the study of microbes. Koch, on the other hand, was an obscure country doctor in Germany. His wife managed to save enough money to purchase him a microscope. It was not long before the miracles which it opened up became his absorbing interest. Independently of Pasteur and one year before, he demonstrated that the disease called anthrax was caused by a certain bacillus, which could be obtained from animals suffering from the disease. When grown in pure culture and injected into animals, it invariably produced the same disease, establishing for the first time that a microbe was the specific cause of a human disease. (See fig. 11.)

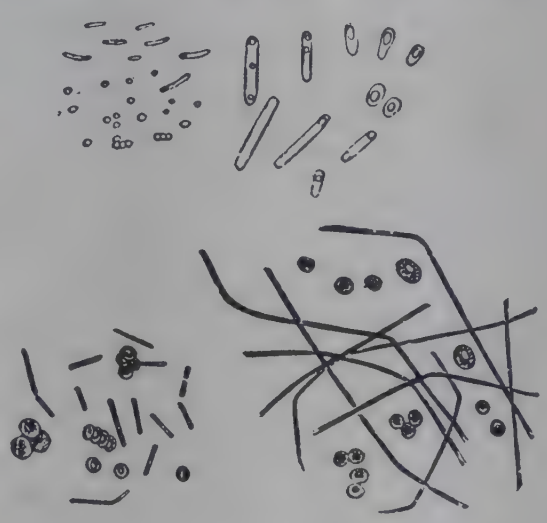


FIGURE 11

Koch's drawings of anthrax bacilli. (After Conn and Conn.)

Further, Koch advanced bacteriologic technic tremendously by a very simple procedure. Prior to 1882 it was extremely difficult to isolate a single species of bacteria from any given material, chiefly because there usually was more than one species present, and all kinds of microbes flourished in liquids used to support growth. But Koch devised a solid medium for growing bacteria. By the addition of a small amount of gelatin or agar (a Japanese seaweed) to ordinary nutrient fluids they become solidified on cooling just as does dessert jelly (which contains gelatin). When a single microscopic cell multiplies on a solid medium, it produces a speck or colony usually large enough to be visible to the naked eye. This colony can be removed and transplanted into sterilized fluids, and then only the members of that single

bacterial species will grow, yielding a so-called pure culture. Koch also succeeded in perfecting a method whereby microbes could be studied more carefully under the microscope and permanently photographed. He fixed the microbes to a glass slide by drying and stained them blue or red with certain aniline dyes. By staining microbes Koch was able to study their structure exhaustively, and then photograph them. Years before, however, in 1871 to be exact, Weigert was the first actually to stain bacteria in diseased tissues with aniline dyes. Previously this pathologist had experimented with other dyes, but they did not yield such clear pictures.

Followed a period of prolific bacteriologic research, which in fifteen years resulted in the discovery of the specific microbes causing typhoid fever, tuberculosis, diphtheria, pneumonia, lock-jaw (tetanus), syphilis, yellow fever, and many other infectious diseases. The whole science of bacteriology is but two hundred and fifty years old. But even more astonishing is the fact that its great practical contributions to medicine have all come within the past fifty years — that is, from the time of Koch.

Nor have the historical advances in bacteriology been restricted to medical problems. Plants as well as animals suffer from diseases. Burrill, an American, in 1878 first described how bacteria caused plant disease, and isolated the organism causing fire-blight, a disease which attacks apple- and pear-trees. Fungi or moulds, the lowest form of plant-life, are prime offenders in causing plant diseases. As early as 1853, de Bary, a German, had indicted moulds as the direct cause of the rust and smut diseases of grain, and then described the nature of the mould causing late blight in potatoes. Kühn, another German, published in 1858 the first text-book in a new science, phytopathology — dealing with the causal agents of plant disease. (See fig. 12.)

Moulds are responsible for human as well as plant diseases. This was first discovered in 1839 by Schönlein, who described the mould causing the formation of scutula, cup-shaped crusts, at the roots of the hair (usually of the scalp). In the same year Langenbeck described the mould causing thrush, a disease peculiar to the mouth, in which membranous areas appear on the tongue. Ringworm and eczema have since also been shown to be

of mould origin. Yeasts, too, are the cause of human diseases, as shown by Busse in 1894.

There remain another group of single-cell organisms, the simplest form of animal life, the protozoa, to be considered as a factor in producing disease. To Lösch of St. Petersburg belongs

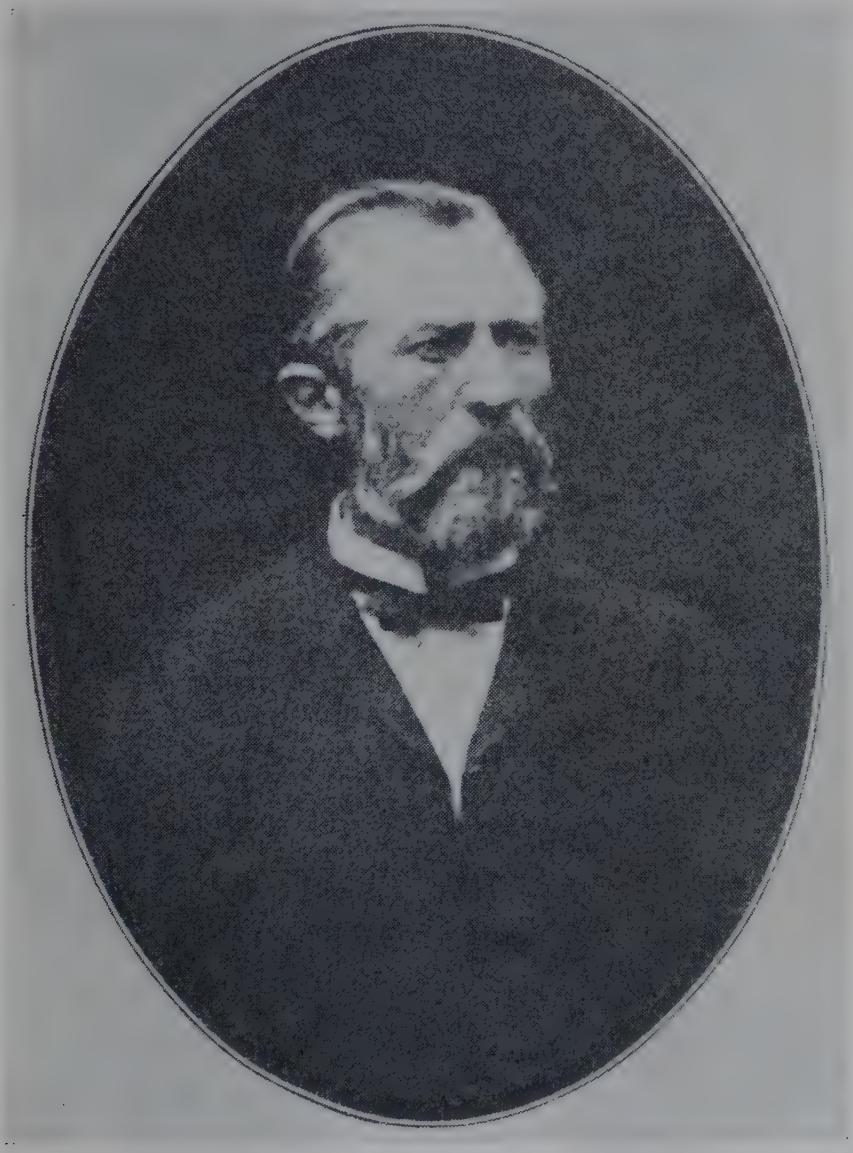


FIGURE 12

Heinrich A. de Bary. (*After Locy.*)

the credit for the first precise description of the amœba causing amœbic dysentery, a scourge of the tropics. Trypanosomes, another kind of protozoa, causing blood infection in man and beast in the tropics, achieved notoriety when Bruce, in 1894, demonstrated them in the dreaded tsetse-fly disease of Zululand. Five years before, in 1889, the great American bacteriologist Theobald Smith discovered the fact that Texas fever of cattle was not only caused by a protozoon, but transmitted by the bite

of the lowly tick (an insect). The best-known protozoon disease, however, is malaria. Laveran (see fig. 13) in 1880 described its nature; Ross and Grassi divide the credit for having shown that it is a mosquito-borne disease. The last word in the discovery of such obscure diseases as Oroya fever has just been said (1926) by

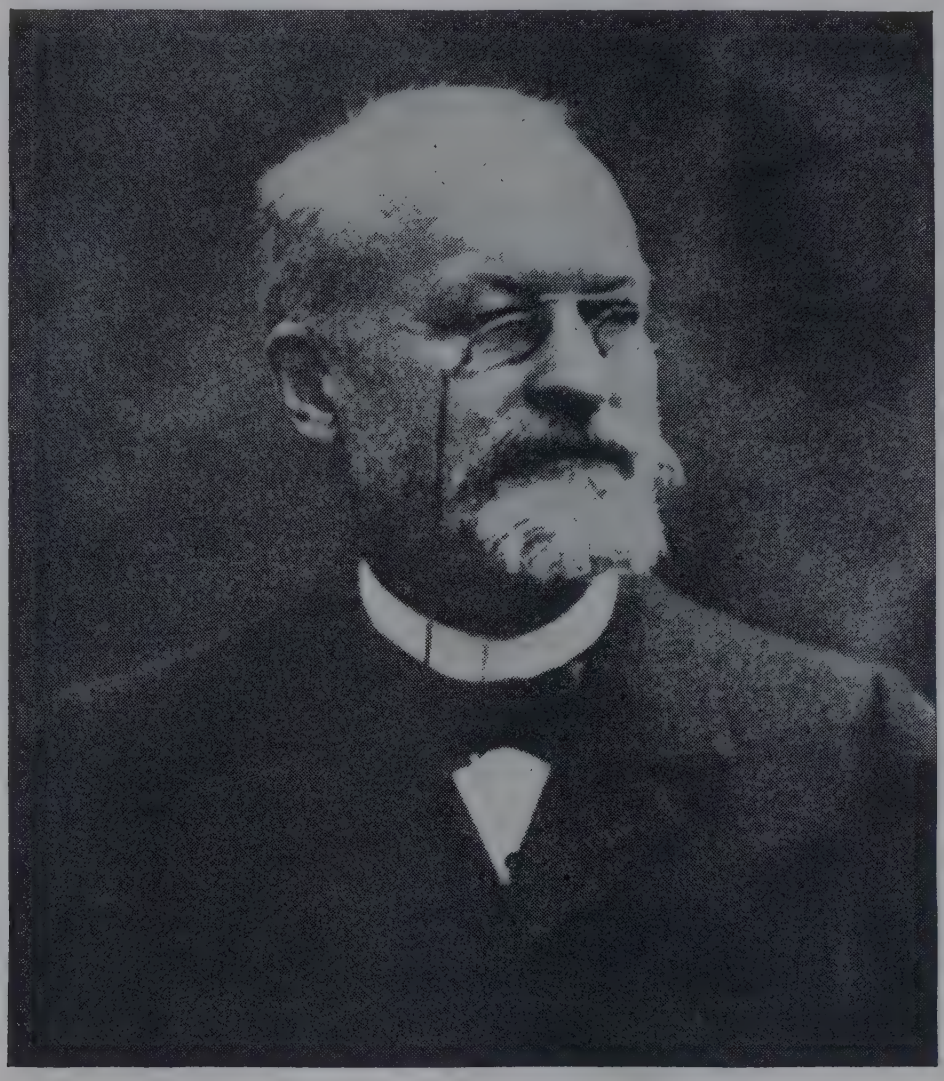


FIGURE 13

Laveran, discoverer of the cause of malaria. (After Deschiens.)

Noguchi, of the Rockefeller Institute, who is also famous for his discovery of the microbe of yellow fever and for his contributions to bacteriological technic. (See fig. 14.)

And now Noguchi, too, is dead — a martyr to the disease he was investigating on the Gold Coast of Africa in 1928. In spite of ill health and in defiance of the counsel of his best friends he undertook the arduous expedition to Accra to investigate the relation between South American and African yellow fever. Two days before he was scheduled to return home with his studies completed, he succumbed to the disease on whose extermination

he was intent. Noguchi's contributions to the science of infectious diseases have brought him and the Rockefeller Institute for Medical Research undying glory. He was born in Japan in 1876 and received his medical degree there at the age of twenty-

FIGURE 14

Noguchi, the famous Japanese bacteriologist, late of the Rockefeller Institute.

one. After serving in hospitals for three years, he came to the United States, beginning his career at the University of Pennsylvania. The Rockefeller Institute for Medical Research called him from the Carnegie Institution in 1904 and he remained an active member of the staff until his death.

Meeting Noguchi in his laboratory, while he manipulated his

microscopes and test-tubes, one was struck at once by a dynamic force rushing at top speed with absolute precision and radiating an inexhaustible energy. His capacity for work was positively overwhelming. The long list of his scientific papers bears ample testimony to his amazing productivity.

Noguchi was the first bacteriologist to succeed in the artificial cultivation of the spirochæte responsible for syphilis. In order to gain this end it was necessary to devise an altogether original technic, which has as its essential features an especially long, narrow cotton-plugged test-tube at the bottom of which is placed a small piece of freshly excised rabbit kidney (free from microbes); some ascitic fluid (tapped from the abdomen of a dropsy patient); and a layer of vaseline to keep out free oxygen. Body fluids offer excellent nutritive elements to microbes, so that it is not difficult to see the necessity for ascitic fluid. But why the bit of kidney, which seems to be the crux of the method? The cells of the kidney, as of any other organ, require oxygen. Consequently, these kidney cells use up the oxygen present in the medium, thereby rendering it anaerobic. This condition favours the growth of the spirochæte. The kidney tissue is also thought to possess certain other indefinable but definitely advantageous properties.

Noguchi also introduced a special test for syphilis, known as the luetin test, and wrote text-books on this general subject, entitled *The Serum Diagnosis of Syphilis and Luetin Reaction* and *The Laboratory Diagnosis of Syphilis*. Finally, he shares with Moore credit for the discovery of syphilitic microbes in the brains of general paralytics. This represents one of the greatest advances in our knowledge of the causes of insanity, for at the time that Noguchi identified the spirochæte, general paralysis was regarded as one of the most hopeless forms of insanity. By pointing out that general paralysis was not primarily due to psychic derangement, but followed syphilitic infection and the definite invasion of the central nervous system by *Spirochæta pallida*, Noguchi and Moore paved the way for the successful treatment of the malady and stimulated the bacteriologic approach to other forms of insanity. Throughout the world Noguchi is recognized as the foremost authority on spirochætal organisms.

Other noteworthy contributions made by him include the

preparation of a bacteria-free vaccine for smallpox, and studies in infantile paralysis, rabies, snake venom, trachoma, Rocky Mountain spotted fever, Leishmanias, etc. The *Journal* of the American Medical Association has said in tribute to him that "to trace his romantic career involves a consideration of infectious diseases throughout the world." Not only was he the recipient of many honorary degrees and medals, but royal hon-

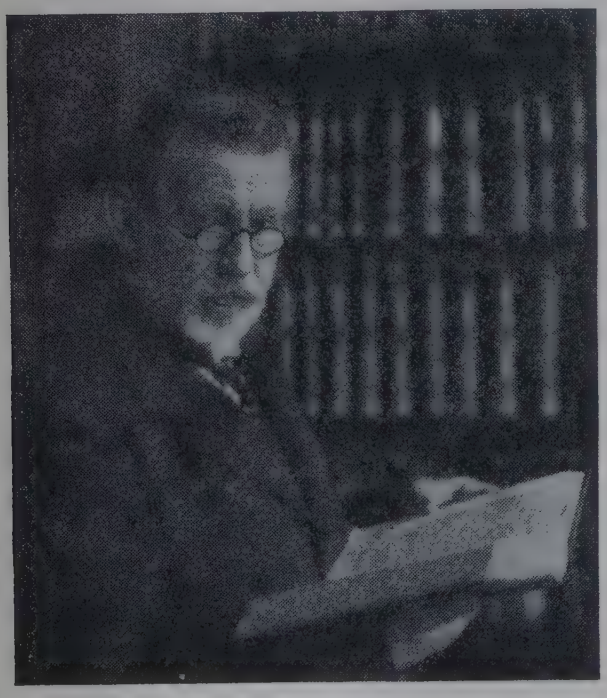


FIGURE 15

Ehrlich, immunologist and discoverer of antisyphilitic drugs. (After Deschiens.)

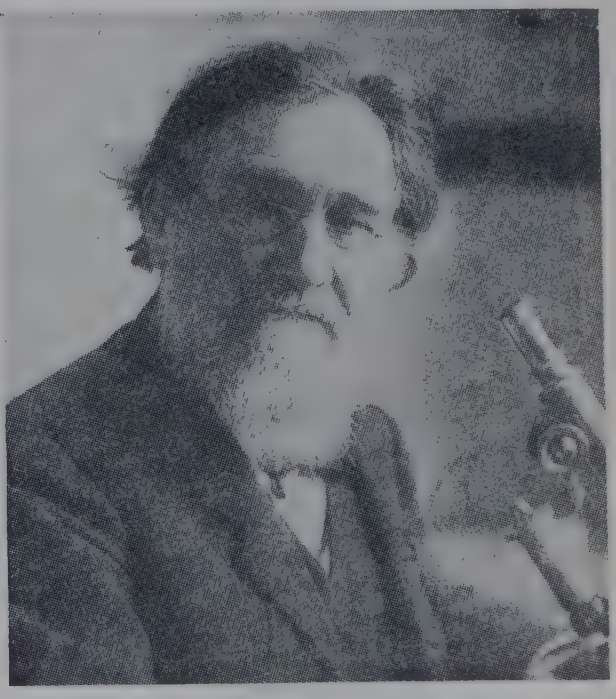


FIGURE 16

Metchnikoff, champion of white blood corpuscles and sour-milk therapy. (After Manuel.)

ours were bestowed upon him by Japan, Spain, Italy, Sweden, and Denmark. Noguchi without question ranks among the great bacteriologists of all time.

Bacteria, moulds, yeasts, protozoa, all cause disease. How, then, is the body protected against them? Why is it that we are not all diseased, since the unseen invaders surround us on all sides? He is indeed a rare individual who can boast that he has never been infected. The wonder is that infections are not more prevalent than they are. There are many theories to account for our escape from bacterial diseases. The two theories which have had the greatest influence on the development of this branch of bacteriology, called immunology, have been those of Ehrlich (see fig. 15), with his chemical explanation, and of Metchnikoff (see fig. 16), with his discovery of phagocytes, which destroy invading

microbes. Each theory has had its adherents and antagonists; today it is felt that neither is an altogether satisfactory explanation of a very complex phenomenon.

The story of bacteriology is the story of its great men. From van Leeuwenhoek to Noguchi each is deserving of the tribute which Charles Singer has paid to Roger Bacon: "Summed up, his legacy to thought may be regarded as accuracy of method, criticism of authority, and reliance on experiment — the pillars of modern science."

Chapter II

BACTERIA AND THEIR ENVIRONMENT

I. BACTERIA: WHAT THEY ARE

Bacteria are among the smallest and simplest organisms known, each consisting of a single cell, visible only through the microscope. Small as it is, each cell reproduces by dividing in half to form two cells. It is extremely difficult to visualize the size of the average bacterial cell, for it is only about 1/25,000 of an inch long. Following the usual formula for presenting statistics: it would take a million bacteria placed end to end to cover the length of a yardstick, but at the number which would be required to circle the globe, the pen runs dry. Dealing with such large numbers of organisms, the bacteriologist applies a special unit of measurement, the micron, designated by the Greek letter μ to express bacterial sizes. The micron is about 1/25,000 of an inch (1/1000 of a millimetre, to be exact). Typhoid-fever bacilli, for example, are from 1 to 3 μ long; influenza bacilli are about 0.5 μ long (which is 1/50,000 of an inch). Nor is their weight anything to boast of. It would require 15,000,000,000,000 typhoid-fever bacilli to balance an ordinary teaspoonful of water. (See fig. 17.)

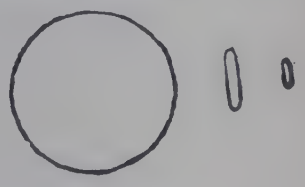


FIGURE 17

Relative size of blood corpuscles, at the left; typhoid-fever bacilli, centre; and influenza bacilli, at the right. (After Jordan.)

In a blizzard all snow-flakes look alike. Under the microscope they are shown to have many different shapes. Just so with bacteria. They are conveniently described as spheres, rods, and spirals. When bacteriologists talk shop, the spherical type is referred to as a "coccus," the rod as a "bacillus," and the spiral as a "spirillum." Of the known bacteria the rods, or bacilli, predominate. As long ago as 1900, Migula listed 833 different bacilli, 343 cocci, and 96 spirilla, or more than twelve hundred different species. Bacteriologists are for ever describing new species, so that

many additions have been made since, but roughly in the same proportion. There are also the so-called higher bacteria (*trichomycetes*), of branching character, which are somewhat larger than the bacteria just described.

In general, bacteria breed true to type. That is to say, cocci perpetuate spheres; bacilli, rods; and spirilla, spirals. But under certain circumstances, as when the environmental conditions are unfavourable, irregular degenerative (involution) forms occur. Thus the diphtheria bacillus, ordinarily a slender rod, when grown in the laboratory for some time, may take on a branching appearance. Similarly, other longer rods, like those which sour milk, may become so short as to appear almost spherical.

Every microbe, like every animal, grows from birth to a maximum size which is constant for its species. In animals reproduction is essentially sexual. A bacterium reproduces, when it has attained its maximum size, by dividing transversely into two equal cells. Then each cell divides again; and so it goes, at a rapid rate. The most astonishing feature of this performance is the rapidity with which the cell matures and is consequently ready to divide. *Homo sapiens* wastes some twelve to fifteen years from birth to reproductive activity. Bacteria require only from twenty to thirty minutes. How prodigious the progeny! Even if a bacterium multiplied once an hour, within twenty-four hours there would be 17,000,000 descendants. And within the next twenty-four hours each of these would produce 17,000,000 more. In three days the descendants would weigh 18,000,000 pounds and in five days at this rate all the oceans of the world would be filled with bacteria.

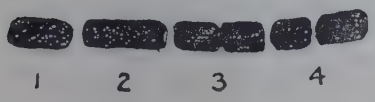


FIGURE 18

Successive stages (numbered) in the multiplication of bacteria by fission (elongation and division). (After Conn and Conn.)

But bacteria, like men, are their own worst enemies. The waste products they produce, such as acids, kill them. One is reminded of submarine disasters in which the unfortunate victims are killed by the carbon dioxide they exhale. A continued geometric progression is thus thwarted. Otherwise bacteria would soon become the sole inhabitants of the earth. (See fig. 18.)

What is a bacterium? It is a mass of cell-substance or protoplasm, much like that which composes the cells of the human

body, usually encompassed by a delicate cell-membrane and surrounded by an envelope or capsule — something like a coconut, let us say. The exact nature of the inner cell-substance has long been a matter of controversy. The consensus of opinion is that the bacterial cell is simpler than all other plant and animal cells in that it has no definite nucleus, or central body, but contains nuclear substance in a diffused state.

Many bacteria, particularly rods and spirals, have the capacity of independent movement by virtue of certain fine hair-like appendages, called "flagella," which whip at the surrounding medium and propel the organism. The number of flagella may vary from one or two to more than eight. Under the microscope an aggregation of different bacilli with their outspread flagella looks for all the world like a flotilla of college crews: eight-oared, four-oared, two-oared; with a liberal sprinkling of canoes, single-and double-paddled. (See fig. 19.)

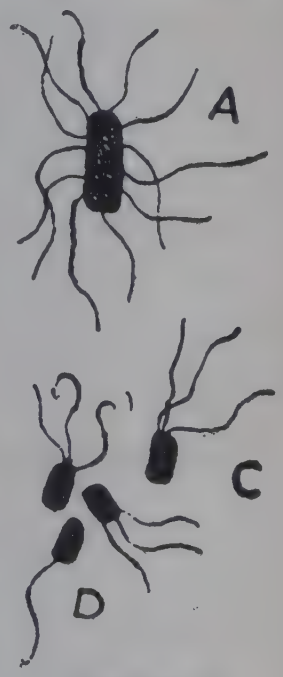


FIGURE 19

Flagella — the bacterial organs of locomotion. A, peritrichic; C, polar; D, single polar. (After Conn and Conn.)

The position of the flagella serves to differentiate certain species. Thus peritrichous flagella, such as belong to the lockjaw bacillus, are flagella which surround the rod. Polar flagella are those which are at the ends of the rods, either singly or in tufts. By means of its flagella, the typhoid-fever bacillus can travel two thousand times its own length in an hour. The cholera spirillum can attain forty-five times this speed over short distances, which makes the fastest human being a slow-moving creature by comparison. Under the microscope all bacteria in fluid preparations seem to oscillate each about a given point. But this is a purely physical phenomenon, called "Brownian movement," bacteria being specks of matter driven by the molecules in the drop (due to kinetic energy). This movement is as different from true motility, where the organism actually moves from one point to another, as is the newest dime-covering Charleston from the old-fashioned, ground-consuming waltz.

Some bacteria, chiefly bacilli again, possess not only motility,

but also the capacity to produce spores. The latter withstand unfavourable environmental conditions such as excessive cold and heat, dryness, etc., by means of their thick covering. The spore itself, which is round or oval, is formed within the cells of the bacillus. It assumes a constant position for each species. Thus the lockjaw bacillus (tetanus) carries the spore at one pole and therefore gives the appearance of a drumstick. The spore really represents a resting stage of the organism, corresponding to the hibernation of certain mammals. The spore can germinate when the environment becomes favourable, thus continuing the propagation of the species. It is not to be presumed, however, that in the life cycle of any spore-bearing bacillus one finds either all living forms or all spores, for usually there is a varying mixture of the two. In fact, the presence of a few spores characteristically situated is often sufficient to identify a bacillus such as that of lockjaw. In excessively hot and dry summers the tetanus bacilli living in the soil are largely killed off and the spores, because of their thicker envelopes, alone remain. They may lie dormant for months or even years. Walking barefoot along a dusty road, you cut your foot on a jagged stone. Tetanus spores enter the wound. The blood offers them moisture, the temperature is favourable. They germinate; from each spore comes a bacillus; the battle for life is on. (See fig. 20.)

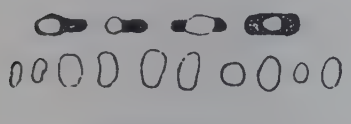


FIGURE 20

Spores of bacteria, showing different forms and location within bacteria. (After Conn and Conn.)

What goes into the making of a bacterium? This is difficult to establish, for the chemical composition varies greatly from species to species, as well as within the species itself, depending upon the kind of food, among other important factors. Bacteria, like all living things, contain water chiefly, as much as from eighty to eighty-eight per cent. Salts (mainly phosphorus, sulphur, potassium, chloride, and calcium, with smaller amounts of magnesium, iron, silica, etc.), fats, proteins, and carbohydrates are also to be found upon analyses of large numbers of bacteria. Our knowledge of the chemistry of bacteria is rather general; accurate details as to the chemistry of each bacterial species are still wanting. The day will doubtless come when precise methods will be devised for establishing the true nature

of these minute living organisms. In a short space of time much has been learned, to be sure, but still more remains unknown.

It is even more difficult to classify bacteria than human beings. Any attempt is more likely to result in further confusion than in clarification, because of the lack of adequate standards. Anthropologists encounter similar difficulties in dealing with mankind, and if one follows the modern tendency, one will not make the mistake of drawing any hard and fast distinctions. There are two general points of view from which bacteria may be regarded. What bacteria do — their physiological activities — is of great practical importance. That might serve as one basis of classification. But experience has taught that this is really inadequate, because there have not been enough criteria devised to differentiate bacteria. The more satisfactory basis for classification, therefore, has been form (morphology). Yet there is much divergence of opinion concerning the status of many species. One sinks or swims with one's prejudices.

The true bacteria (as opposed to the higher bacteria, which need not here be further classified) are usually divided into three families; much as one would characterize men and women into fat, lean, and wriggly types:

Coccaceæ [1] — the spherical forms
Bacteriaceæ [2] — the rod-shaped or oval forms
Spirillaceæ [3] — the spiral forms

[1] *Coccaceæ*, or spherical forms, rarely produce spores or possess motility. They are usually subdivided into four genera, the first two being best known: (1) *Streptococcus;* (2) *Staphylococcus;* (3) *Micrococcus;* (4) *Sarcina*. The streptococci form chains; the staphylococci form clusters or sheets; the micrococci form squares or sheets; the sarcinæ form cubical packets.

[2] *Bacteriaceæ* are rods, longer than they are wide. The following genera are widely described: (1) *Bacillus* — produces spores and has surrounding flagella; (2) *Clostridium* — spindle-shaped because of large spore and is unable to grow in the presence of free oxygen (anaerobic); (3) *Pseudomonas* — with single flagellum, seldom producing spores; (4) *Bacterium* — without spores, or non-motile.

[3] *Spirillaceæ*, spirals or comma-shaped bacteria, are usually divided into: (1) *Spirosoma* — large, non-motile spirals in gelatinous masses; (2) *Microspira* — short, motile, comma-shaped bacteria (sometimes called "vibriones"); (3) *Spirillum* — long, corkscrew threads with flagella. (See fig. 21.)

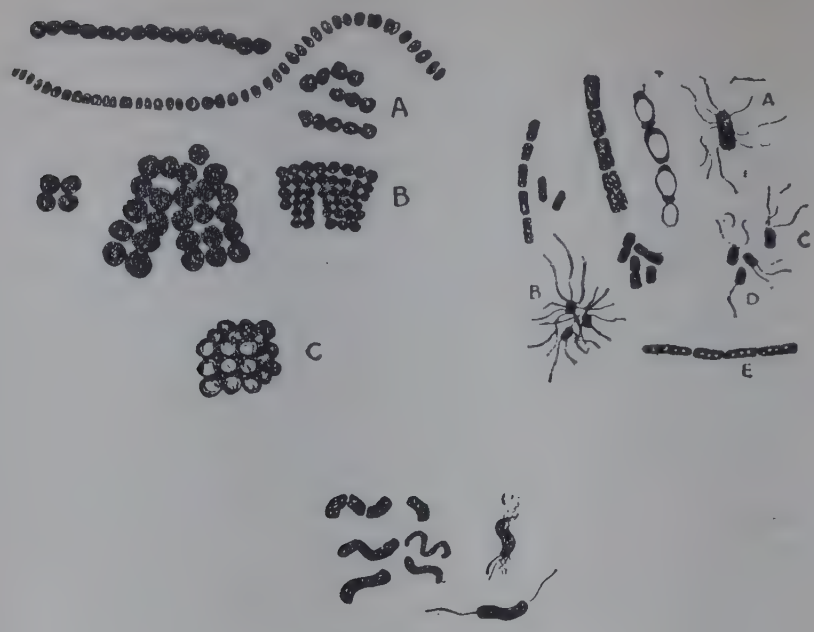


FIGURE 21

Different kinds of bacteria. Cocci at the left: A, streptococci; B, micrococci; C, sarcina. Rods at the right, rods, and flagella, as in Fig. 19. Below, spirilli, with and without flagella. (After Conn and Conn.)

2. HOW BACTERIA LIVE

Like men, bacteria are finicky about their food. Both have their irreducible requirements — which are not dissimilar. The chemical elements entering into the composition of bacteria have just been enumerated. Obviously these must be present in the food-supply. All living organisms are organic; that is, they contain carbon as an essential ingredient. They also contain inorganic substances (without carbon). Animals cannot build up their own organic compounds; they must ingest plant or other materials which contain organic substances. How, then, do plants obtain their organic matter? The green colouring-matter (chlorophyll) utilizes sunlight as a source of energy to manufacture organic matter out of carbon dioxide (the gas which human beings exhale) and water, in the process known as "photosynthesis." Anyone who has ever had the slightest serving of biology spread before him is at a great disadvantage in trying to remember "photosynthesis" because biological information has a disconcerting way of running together like lava, only to cool into an amorphous mass. How much easier it is to dissect the word: "photo" means "light"; "synthesis" means "building up"; *ergo*, building up by means of light. Bacteria, however, have no

green colouring-matter, and sunlight is detrimental to their existence. Nevertheless, by some mysterious power some bacteria have the unique capacity of transforming atmospheric gases into organic or carbon-containing combinations. The so-called nitrogen-fixing bacteria which form nodules on the roots of plants such as clover and alfalfa are the most economical organic nitrogen factories known.

Food is not always readily available, even to bacteria, particularly if it is too concentrated; it must be diluted with fluid — in other words, have the proper concentration. How often is ordinary cow's milk, otherwise considered a perfect food, too "rich" for a baby with a sensitive digestive system! The milk must be thinned with water. And the housewife knows that a thick sugar syrup preserves fruit from spoiling, while a thin solution is speedily attacked by microbes and thereby contaminated. In addition to concentration the degree of acidity or alkalinity is of significance. While this varies for different species, most disease-producing bacteria prefer a very slight acidity.

Bacteria from the standpoint of their mode of existence are commonly grouped in two categories: the harmless microbes being called saprophytes, and the harmful microbes parasites. Saprophytes attack dead organic matter — that is, dead plants or animals. Parasites thrive within the living substance of plants or animals. One thinks of the tapeworm as a parasite; but equally tenacious is the malarial organism, or any one of a host of microbes which prey upon the human body. Any living organism resents the intrusion of another, and the means of defence against invasion are many and varied. By overcoming such resistance, however, a microbe can attach itself to, or get within, a living organism, making the latter its unwilling host. Instead of foraging for its victuals the invader placidly permits its host to perform all such labours and appropriates what it needs. In other words, it assures itself a constant source of food already prepared. Obviously, all disease-producing microbes belong in the category of parasites. When the exigencies demand it, nevertheless, many of the parasitic bacteria can lead a saprophytic existence and vice versa. Some parasites, however, become so dependent that without a suitable host they perish. Many a sociological concept has been built on a less secure analogy.

In addition to inadequate food-supply, bacteria require a certain amount of moisture. It is well known that most bacteria are readily killed by air-drying, although some forms, like the tubercle bacillus, are quite resistant to drought. Water is essential to the existence of bacteria. Its total absence results in death.

The relation of bacteria to oxygen-supply is most complex. Bacteria can be divided into two main groups on this score. There are first those bacteria which require free oxygen for their development, called "aerobes," and secondly there are those which thrive in the absence of free oxygen — as in a hermetically sealed vessel — called "anaerobes." Thus we have obligatory aerobes, and obligatory anaerobes. A number of microbes, however, are not so fussy; when there is free oxygen, well and good, and when there is no free oxygen, well and good. Thus they also fall into two groups — namely, the facultative aerobes and facultative anaerobes. The former prefer free oxygen, but can exist without it; the latter prefer no free oxygen, but can exist in its presence. All the permutations and combinations of microbes and the presence and absence of oxygen may be found to exist in nature.

Light, particularly direct sunlight, is harmful to bacteria. In fact, it is the cheapest agent for killing microbes. Direct sunlight is a hygienic necessity and therefore a valuable adjunct to the sick-room. With this in mind, modern hospitals are being built so that all rooms are outside rooms.

Chemicals of various kinds act as poisons to microbes; these will be described in a succeeding chapter. A word may be said in this connexion of the harmful effect exerted by some kinds of bacteria on their fellows. This may be direct, as in the inhibition of the plague bacillus by cocci; or indirect, as in the overgrowing of all other bacteria by certain milk-souring bacilli capable of surviving in the more acid environment. Occasionally microbes are of mutual benefit and live together happily in what is called a state of symbiosis. For example, aerobic bacteria by consuming all the free oxygen thereby make conditions favourable for the growth of anaerobic bacteria.

No description of what bacteria are and how they live can be complete, because of the enormous number of species. Exhaustive investigation of a few related species is a life-work in itself, and the facts are frequently complicated and conflicting. The

best that can be offered is a general survey which takes into consideration certain important features. The activities of bacteria are multiple. On the one hand, they are destructive, breaking down substances to a simpler form; on the other hand, they are constructive, building up complex substances from simple constituents. These activities are present throughout nature, in every aspect which concerns man. Their usefulness in agriculture and industry should be recognized. Their rôle in disease is universally feared. Bacteria are rightfully more often regarded as foes than as friends of man. Let us therefore inquire into one of the most important agents for their destruction — namely, heat.

3. HOW TO DESTROY BACTERIA

In the relation of bacteria to their physical environment, temperature plays a very important rôle. As with all living things, there is a temperature range at which they flourish best, called the "optimum" temperature for growth. The optimum temperature varies for different species, but remains constant for any given species. Witness the Eskimo and the Senegambian. The highest temperature which permits of growth is known as the "maximum," beyond which lies the *thermal death point*. The lowest temperature which will permit of growth is known as the "minimum," and if they do not like it, the bacteria are likely to have as much luck as the average New York tenant when he complains to the janitor. As a rule, the optimum range of temperature for the growth of disease-producing parasites is that of the human body: about 98.6°F. What perfect adaptation! Not only does man fall easy prey to his antagonists, but his body becomes a culture tube for more generations of microbes. Saprophytes, more likely to be friends than foes, find their optimum temperature between 75° and 85°F.

Bacteria which do not produce spores are more easily killed than those which do, for they do not have the protection of a thickened covering that withstands adverse conditions. Ten minutes' exposure at 150°F. is the thermal death point for non-spore-bearers. To kill the more resistant spore-bearing forms it frequently requires some 100°F. or more beyond this point. Fortunately, the thermal death point for water-polluting bacteria is

fairly low, about 140°F., so that boiling water (212°F.) makes it safe for human consumption.

Most bacteria are more resistant to cold than to heat. But some thermophilic, or heat-loving, bacteria have been found alive in natural hot springs at a temperature as high as 192°F. Again, it is not the sun alone which tints the snow in the high Alps and Arctic regions, but the delicate colouring is actually caused by microbes. These extremes indicate the diversity of their habitat. Some bacteria have been exposed to the temperature of liquid hydrogen, about 418°F., and even then, strange to say, have survived.

The most effective and extensively used physical agent for the complete destruction of microbes is heat. There are, however, three important factors to be considered in the application of heat — namely, the degree of temperature, the length of time, and the nature of the object to be sterilized. Regarding the first of these, different degrees of temperature kill different bacteria since they have different thermal death points. But it is also well to remember that protracted exposure to a moderate degree of heat destroys bacteria as effectively as a short exposure to a very high degree of heat. There are two methods whereby heat is ordinarily employed for the destruction of microbes: the first to be considered is dry heat; the second, moist heat. The choice of either depends largely upon the object to be sterilized.

FIGURE 22

Bunsen burner. (After Park, Williams, and Krumwiede.)

Dry heat may be applied by direct flame or indirectly in hot air chambers. The direct flame from a gas-burner (see fig. 22) or alcohol lamp is used in the laboratory to sterilize platinum needles (used for transferring small amounts of bacterial suspension) or the mouth of a test-flask before or after it is opened. Direct flame is also utilized for burning objects such as rags or cloths from the sick-room.

Most articles, however, are too valuable to be burned merely for the sake of destroying microbes which they harbour. For these sterilization by hot air is therefore more desirable. This is accomplished in a hot air oven or chamber, which consists of a metal chest heated by a gas flame or electricity. The required

temperature, usually about 320°F., is maintained by a special regulating device. In one hour sterilization is effected. This method is universally employed for sterilizing laboratory glassware and articles which might be injured by moist heat. (See fig. 23.)

Moist heat is more destructive to microbes than dry heat of the same degree of temperature — among other reasons, because of its greater power of penetration. Prior to extinction the bac-

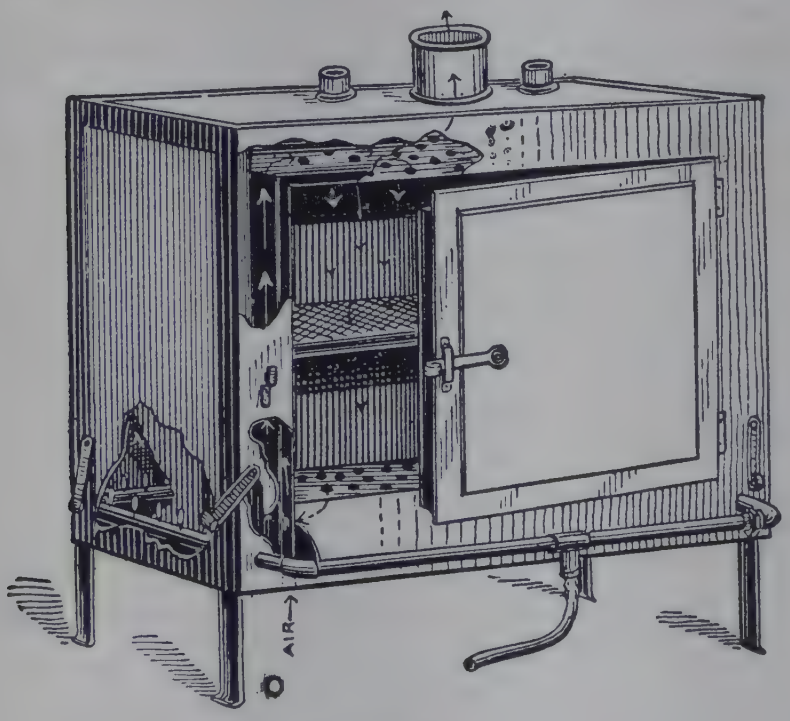


FIGURE 23

Hot air sterilizer (Lautenschläger). (After Jordan.)

teria doubtless remark: "It's not the temperature; it's the humidity." Moist heat may be applied as boiling water, streaming steam, or steam under pressure.

Boiling in water for five minutes kills all living microbes. Consequently boiling water is most frequently employed for sterilizing surgical and dental instruments, syringes, etc. To destroy spores (the more resistant and resting stage of bacteria) one or two hours of boiling may be required.

When moist heat is applied as live or streaming steam, a special receptacle called an "Arnold sterilizer" (see fig. 24) is usually employed, although an ordinary wash-boiler may suffice. The principle underlying the Arnold sterilizer is the vaporization of water from a reservoir heated by a gas flame through a narrow neck so that steam is continually poured into a large covered

chamber above. The temperature of live steam is 212°F. The Arnold sterilizer is used for the "fractional" or "discontinuous" method of sterilization, which is a subtle way of drawing bacteria out of their shells, so to speak. The material to be sterilized containing microbes is placed in the chamber for thirty minutes on each of three successive days. During the first day's heating all the living microbes are killed, but if spores are present they will survive. In the interval which elapses before the second day's heating these spores will germinate into living organisms, which will succumb during the second heating. The process is repeated and finally, after the third day's heating, complete killing is usually effected. The fractional method of sterilization may also be utilized at a lower temperature for a longer period of time and a greater number of days for albuminous materials, such as blood-serums, which would otherwise be extremely coagulated at the boiling-point.

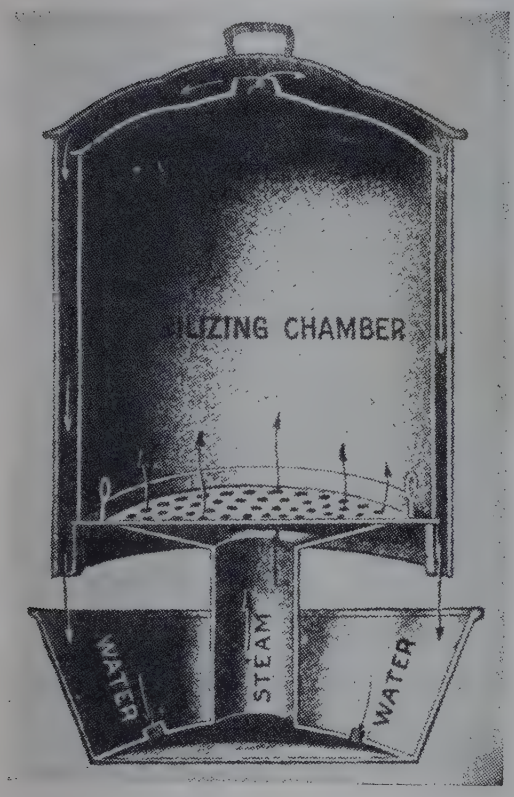


FIGURE 24

Arnold sterilizer (steam at atmospheric pressure). (After Jordan.)

Steam under pressure is the most effective method of heat disinfection and the most popular. No hospital is without its autoclave. And the ultra-modern barber-shop boasts a large shiny nickelled or brass barrel mounted horizontally on firm uprights. The barrel has a door which is well reinforced and held in place by the pressure within or by special clamps or a large screw-wheel. The operation of the autoclave (see fig. 25) is not difficult. Objects to be sterilized are placed within the barrel, and the door securely fastened. Steam is let in, or generated in the chamber by the application of heat (gas or electric) to water. The steam is then subjected to further heating, which causes expansion, and great pressure is exerted, usually fifteen pounds per square inch, on the objects in the barrel. Or, in terms of degrees Fahrenheit, a temperature of 250° is developed. Fifteen to twenty minutes is usually sufficient to effect sterilization. The

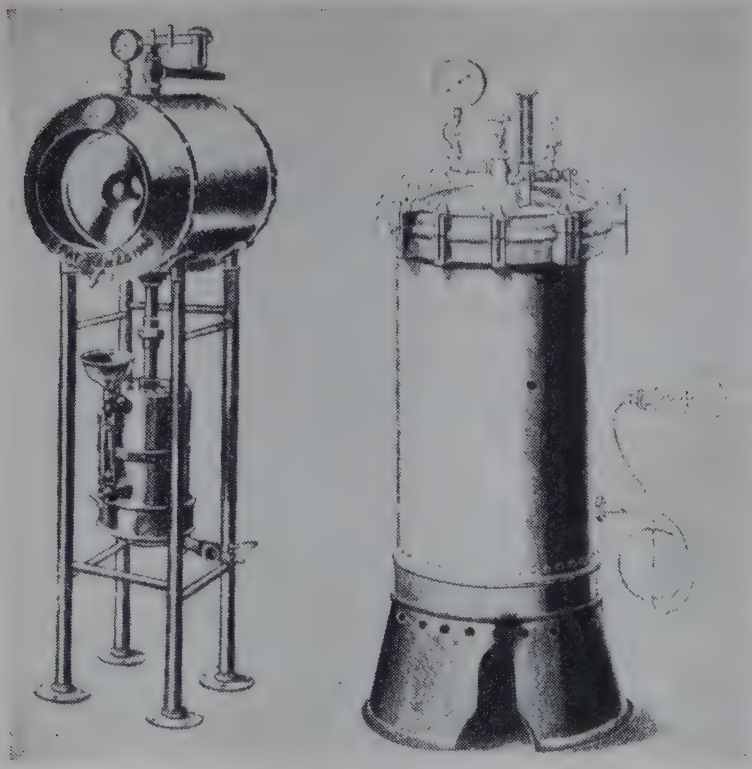


FIGURE 25

Autoclaves (steam under pressure). (After Conn and Conn.)

amount of pressure and length of time may be varied to suit the particular need. Infected materials of all kinds are best sterilized in the autoclave, which has become an indispensable piece of laboratory apparatus. It is also used for surgical dressings, towels, etc.

Heat, then, is used for sterilization, or the complete killing of microbes and spores; chemicals are employed chiefly as antiseptics, which merely prevent growth, or disinfectants, which kill harmful microbes.

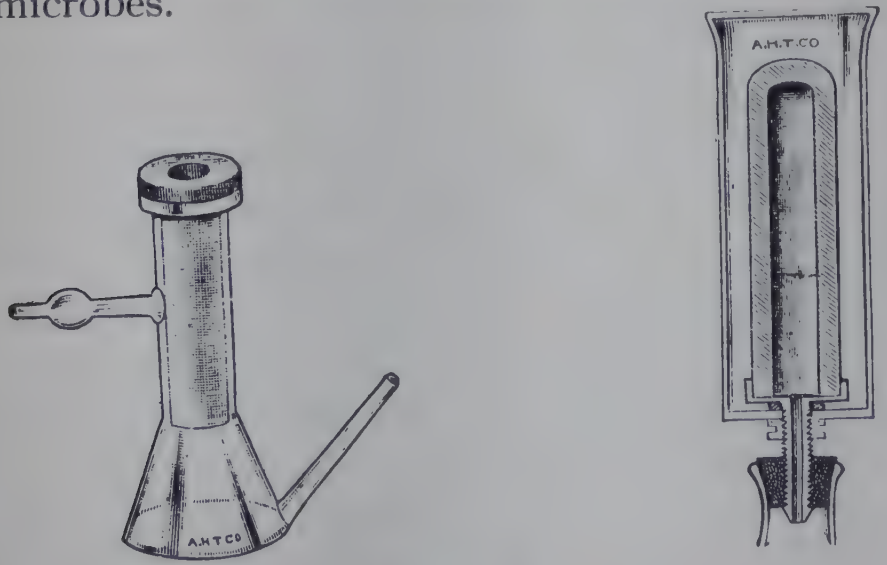


FIGURE 26

Bacterial filters of unglazed porcelain and diatomaceous earth. (After Park, Williams, and Krumwiede.)

There remains one other method of removing microbes from fluids — namely, by the means of special filters. The use of filters for purifying drinking-water is widespread, but those usually employed do not strain out microbes. For this purpose finer filters are required and those employed are usually made of porcelain or some very fine clay material. The pores, invisible to the naked eye, are so fine that they do not permit even microbes to pass, but do let the fluid through, thus effecting sterilization without the use of either heat or chemicals, which are likely to alter the composition of many fluids and serums. (See fig. 26.)

Sterility — freedom from microbes — is the watchword of the bacteriological laboratory. Appreciation of its principles and application of them are a paramount necessity for the laboratory worker, the surgeon, the physician, the sanitarian. "Knowledge is power." All the power at our command is needed for the destruction of microbes — man's invisible enemies.

Chapter III

HOW MICROBES ARE STUDIED

I. MICROSCOPIC METHODS

The telescope annihilates distance, the microscope creates a world. Glibly we speak of microbes, yet how few of us trouble to look at them. Your family physician keeps his microscope handy — perhaps out of sentimentality for the days when he believed medicine to be more of a science than a business, or to impress his patients with his modernity. It will give both of you a thrill to wipe the dust from the eyepiece, to peer through the tube and focus the lens. A little jockeying of the mirror below the stage to get the proper illumination, a slight thrust to the glass slide clamped above it — and, behold! the invisible world is made visible. (See fig. 27.)

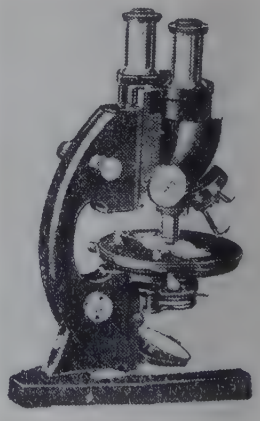


Figure 27
Modern microscope.

Living microbes may be examined under the microscope "in the altogether," suspended in a drop of water (or in any other suitable medium), or they can be killed and stained to bring out finer details of their structure. No examination of bacteria is more important to public health than that of drinking-water. How, then, does one proceed to examine a drop of ordinary tap water suspected of pollution? Before commencing, it should be carefully borne in mind that the air and all surrounding objects harbour microbes, so that in order to examine the microbes in the water all others must first be excluded. Therefore all instruments and apparatus used should first be cleaned and then sterilized; otherwise there would be no way of distinguishing the microbes already in the water from those which fall in uninvited.

The description of a technical procedure is always bewildering. Pictures are usually more impressive for one can usually grasp the essentials. Let us, however, follow the steps in the examination of a "hanging drop" (see fig. 28) — which is a

preparation of living, unstained microbes. Thin, flat glass slides are ordinarily used for the study of bacteria, but remember that in this case it is necessary to preserve the drop of water intact, not to let it dry up, as it naturally would if spread out, in which event the bacteria would die off. Consequently, a special glass slide having a hollow, ground out on one surface, is used. Now for the preparation of the drop, of whose elusive population we are about to take a census. By means of a platinum loop, (see fig. 29), which has been held in a gas flame to sterilize it, the drop to be examined is transferred to the centre of a cover-slip. A cover-slip is a very thin square or circle of glass. The cover-slip is quickly inverted over the hollow portion of the glass slide by means of a pair of slender forceps after a

FIGURE 28

Hanging-drop preparation for the microscopic examination of living microbes. (After Park, Williams, and Krumwiede.)

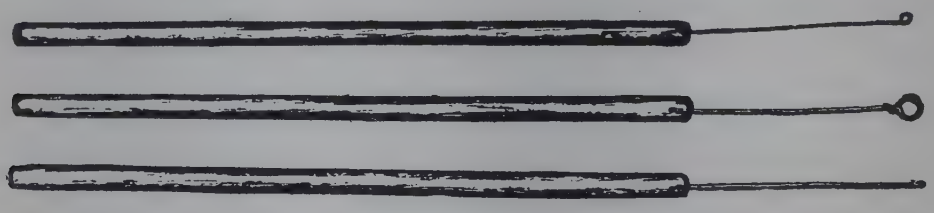


FIGURE 29

Platinum needle and loops mounted in glass. (After Conn and Conn.)

little vaseline is applied to the circular edge of the hollow on the slide to keep the cover-slip closely fixed and prevent evaporation of the drop. The cover-slip is pressed down slightly to make a perfect seal. Then, after clamping the slide on the stage of the microscope, the lens is carefully focused.

Myriads of microbes will be seen swarming throughout the drop. This is the sight that greeted van Leeuwenhoek, the father of microscopy. His microscope was a labour of love, hand-fashioned. A modern binocular microscope with all its trimmings would probably make the dear old man dizzy — and the price, running into hundreds of dollars, would scandalize the thrifty Dutchman; but his scientific ardour could be counted on to overcome all scruples and he would surely marvel at a magnification of over three thousand diameters, which is about ten times the enlargement it was possible for him to obtain.

Living microbes may be studied in the hanging drop as described and also in the hanging block or hanging mass. The latter methods are based on the use of solid nutrient agar (a gelatin-like substance), which supports growth while sealed to the cover-slip on a hollow slide. Thus, under the microscope, one can observe the microbes while they multiply, even as one inspects the intimate affairs of a family of goldfish.

In examining certain living microbes, such as the spirochætes of syphilis, a special dark-field attachment to the microscope is employed. The microbes then stand out like comets in the night. But bacteria are usually best studied dead in fixed film preparations, often called "smears," which are permanent.[1]

There are special methods for staining spores, capsules, and flagella; for spirochætes; for acid-fast bacilli (tubercle bacilli, etc.), so-called because when once stained they retain the dye in spite of attempts to decolorize them with acid; etc. (See fig. 30.) Most important of all special staining technics is that of Gram, who devised a method for the differential staining of bacteria.

Since repeated reference will be made to the Gram stain, it merits description. Films made in the manner outlined above are treated with gentian-violet, which stains them bluish purple. An iodine solution is added and washed off. A decolorizer is added, usually alcohol, which when effective removes the bluish-purple colour. A counter-stain, red or brown, is applied. If the violet-stained bacteria have not been decolorized, they remain bluish

[1] The process consists of the following steps (after H. Zinsser: *A Textbook of Bacteriology*. New York, D. Appleton & Co., 1927): "(1) spreading on cover-slip; (2) drying in air; (3) fixing; (4) staining; (5) washing in water; (6) blotting; (7) mounting." Not all of these steps are self-explanatory. (1) Spreading on cover-slip, for example, means that a thin film, or smear, is made on a cover-slip of the fluid to be studied — or, if it is a solid substance, a small drop of sterile water is added, so that a thin film can be made. (2) When thoroughly air-dried, (3) the film is fixed — that is, made to adhere firmly to the surface of the slide — and the bacteria killed by passing it slowly three times through a gas (Bunsen) or alcohol flame. Chemicals, such as wood alcohol or saturated corrosive sublimate solution, may be used in lieu of heat to fix the dry films. (4) In staining, very weak solutions of basic aniline dyes, such as methylene-blue, gentian-violet, and fuchsine, which colour the bacteria blue, violet, and red respectively, are used so that the detailed structure of the organism may be more clearly discerned. There are a host of other dyes which may also be employed, ranging through all the colours of the spectrum. (5) Washing in water removes any excess stain. (6) Blotting obviously dries the film so that it can be (7) permanently mounted face down on a glass slide with a small drop of Canada balsam. The film, or smear, is thus permanently preserved.

purple and are called "Gram-positive." To this group belong the pus-forming staphylococci and streptococci, the specific organisms of pneumonia, diphtheria, tetanus (lockjaw), tuberculosis, anthrax, etc. If decolorized, the counter-stain shows red or brown "Gram-negative" bacteria, which cause such diseases as typhoid fever, dysentery, cholera, gonorrhœa, etc. (Incidentally, bacteria and especially protozoa can be stained alive as well as when killed and in fixed preparations.) All bacteria, therefore, are easily subdivided into these two major groups; or, to put it another way, the Gram stain serves to differentiate broadly bacteria which when unstained look alike.

FIGURE 30

Capsules surrounding bacteria. (After Park, Williams, and Krumwiede.)

Upon the microscopic examination of fixed films hangs many a medical diagnosis. Inflammation of the throat, for example, immediately arouses the physician's suspicion of diphtheria; but there are bacteria other than the true diphtheria bacillus (*Bacillus diphtheriæ*) which may produce a definite inflammation. Only a culture taken from the throat, together with the microscopic examination of films, can positively establish the bacteria responsible for the infection. Other examples of the value of bacterial cultures in aiding diagnosis are the examination of the sputum or infected tissues of patients suspected of having tuberculosis of the lungs or other organs, and the examination of fæces where typhoid fever is suspected.

2. ARTIFICIAL CULTIVATION

Under the microscope we may examine in a single film preparation either one kind of microbe or several, depending upon the material from which the film was prepared. But tremendous significance attaches to the artificial cultivation of microbes in pure culture — that is, the growth of one kind of microbe apart from other kinds. Pure cultures enable us to study more closely the form, as well as the various physiological and chemical activities, of each micro-organism. Such cultures are best obtained by grow-

ing microbes upon solid media, and to Koch belongs the credit for introducing, in 1881, what is now mere laboratory routine. The coral secreted by a single tiny animal is hard to visualize, but a coral reef offers no such difficulty. Just so with bacteria. A single microbe can be seen only with a microscope, but its progeny on a solid substrate appear as a colony visible to the naked eye. Bacterial colonies, like flowers, are characteristic of the species. Some are large, some small, some round, some oval. They may be regular in outline or irregular, transparent or opaque, white or grey or pink or green. Frequently the appearance of the colony may be sufficient to differentiate one species from another, but more often its characteristics are not so striking as to make classification possible on this score alone.

In order to grow microbes in pure culture on solid media it is first necessary to prepare the media. Absolutely clean glassware is a prerequisite. Thorough washing, therefore, is followed by some chemical agent, such as "cleaning mixture," the common name for sulphuric acid solution containing some bichromate of potash. Test-tubes and flasks or other narrow-mouthed containers, after a thorough rinsing in running water, are dried and plugged with cotton batting (non-absorbent cotton). Finally all glassware is sterilized by hot air for one hour in an oven at 320°F. It is then ready for use.

The food requirements of microbes are much like those of men. To grow microbes artificially the best results are to be obtained by approximating as nearly as possible their natural habitat. All disease-producing microbes, therefore, grow best on media which resemble the composition of the animal body. In general the basis of most of the common laboratory media is meat broth, which is made by infusing lean beef with distilled water. Meat extract is often a satisfactory substitute for less fastidious microbes. The meat broth is usually reinforced with a very small amount (1 per cent) of peptone (an animal protein) and 0.5 per cent of sodium chloride (table salt). But broth, hot or cold, is a liquid, and one cannot distinguish bacterial colonies in liquids. Therefore agar (Japanese seaweed) is added. Agar, like gelatin, causes liquids to solidify upon cooling. Other nutrients, such as different sugars, may also be added to propitiate certain kinds of bacteria. Acid or alkali is introduced to effect the

desired reaction, which differs for different species. Most bacteria prefer a slightly acid reaction, while others have their own individual requirements.

The medium, often turbid, may be cleared while hot with white of egg and filtered through cotton. It is then distributed into glass test-tubes, flasks, etc., in desired amounts. Obviously, throughout the process of preparation, microbes have ample opportunity for gaining access to the media from the air as well as from the ingredients. Consequently they must be killed. This cannot be over-emphasized, because of the ubiquity of microbes. Sterilization is carried out in the autoclave or in the Arnold sterilizer, as previously described. After sterilization, media may be kept several months in the ice-box until ready for use, but will gradually dry out.

Meat broth is often only the base to which other ingredients are added, just as in the preparation of subtle soups. Many different substances are used to furnish food for the growth of microbes: egg, glycerine, milk, potato, different sugars, salts, blood, and blood-serum, bile, etc. Coloured "indicators," or dyes, are frequently added which enable one to follow the changes in colour due to the acidity or alkalinity of the medium resulting from microbial growth. Gelatin, originally used instead of agar for making solid media, is not so satisfactory because it has the disadvantage of being melted by heat at 75°F. or liquefied by certain microbes. Agar is not thus easily made fluid; it has ten times or more the jellying power of gelatin, does not melt much below 140°F., and is not attacked or used as a source of food by certain microbes, as is gelatin. This means that meat broth, for example, containing one per cent agar, is solid when cold, but the solid agar medium can be melted with the application of sufficient heat and poured into another receptacle and will harden again when cool. How is this of value in cultivating microbes, say, from milk? Let us make a slow motion picture of the process:

Heat a test-tube containing sterile meat-broth agar until it is melted. Cool to about 107°F. The experienced bacteriologist presses the tube against his temple and knows that it is the proper temperature when it does not feel uncomfortably hot. If the medium is too hot, it will kill the microbes to be grown; if too cold, the medium becomes lumpy. Sterilize a platinum needle

(with a small loop at the end) by passing it through a flame. Dip it into the milk to be investigated. As the cotton plug of the test-tube containing the medium is removed, flame the mouth of the test-tube, introduce the platinum loop, and rinse the milk in the melted broth agar. This procedure is known as inoculation. Flame the mouth of the test-tube and replace the cotton plug. All this flaming is to kill microbes which may accidentally alight on the materials which are being used to grow only the microbes in the milk. Obviously, if a few microbes from the air fell into the medium, they would grow and it would be impossible to determine which came from the air and which from the milk. Before

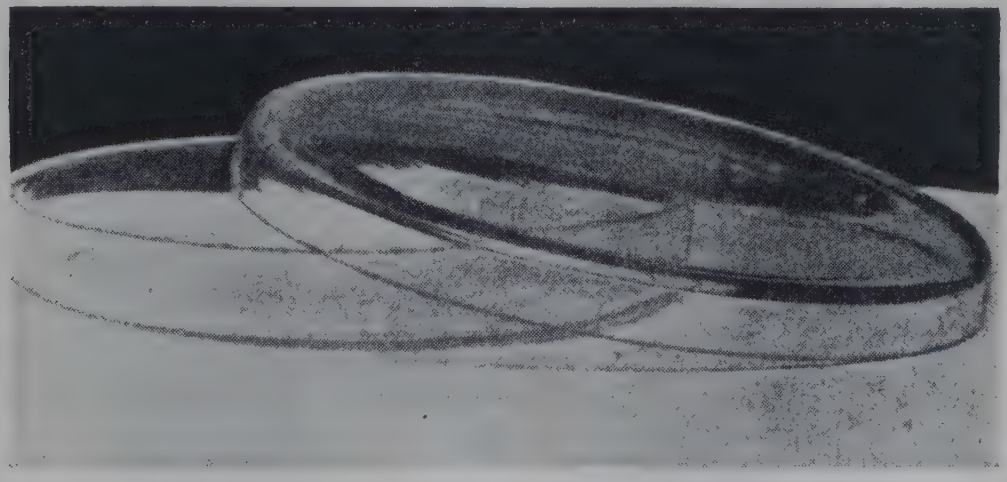


FIGURE 31

A Petri dish (opened). (After Conn and Conn.)

the melted medium, which has been inoculated with the milk, is allowed to cool, it is agitated and poured into a Petri dish. (See fig. 31.) This consists of a round, shallow, glass dish about three and a half inches in diameter, with a similar cover, making a well-fitting glass box. Why grow microbes in Petri dishes when Pasteur and others of his day used flasks? The outstanding advantages of Petri dishes are, first, that they permit the growth of colonies on the surface of a solid medium, which means enhanced visibility, and, secondly, that any single colony can be examined or removed easily. Petri dishes are sterilized by dry heat prior to use, like all other glassware.

To resume: the cover of the Petri dish is lifted just enough to permit the medium to be poured out of the test-tube (after flaming its mouth). If the cover were carelessly removed, microbes from the air would easily gain an entrance. The liquid

medium now cools and solidifies in the Petri dish. The latter is placed in an incubator (see fig. 32), which is a chamber heated by either gas or electricity, usually to a constant temperature of 98.6°F., the optimum for most microbes. Now, each microbe in the medium during incubation reproduces rapidly, forming colonies, which usually become visible in about eighteen to twenty-four hours. They appear as specks on the surface of the medium. (See fig. 33.) These may be more carefully examined with a hand magnifying-glass or even by the microscope. Theoretically each colony or speck represents the progeny of a single individual. Actually, it may not be so pure, and further separation must be made.

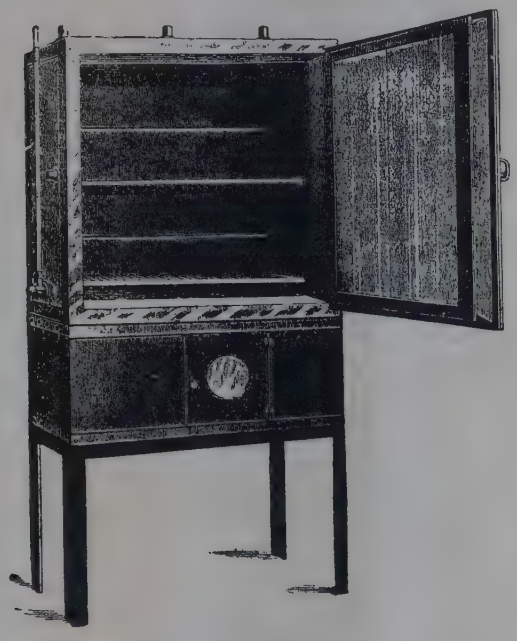


FIGURE 32

Incubator for growing microbes at a constant temperature. (After Park, Williams, and Krumwiede.)

The colonies on the surface of the medium, then, tell us what microbes have been present in the milk. In order to study them more carefully in pure culture, we must "fish" each characteristic colony. For this "fishing" a platinum needle serves as a fishing-pole. The colony is touched by the needle, and the adhering microbes are transferred to a test-tube of sterile meat broth. In the incubator, growth goes on apace. It is like the House that Jack Built. We start with the original microbes in milk. They give rise to characteristic colonies on a solid medium. From single colonies a few individuals are "fished" into broth. They propagate. We now have pure cultures of the original microbes. Each may be perpetuated indefinitely by subculturing further into other sterile media and studied at leisure in film preparations. Likewise subcultures may be made into appropriate media such as sugar solutions or milk to observe the physiological activities of the organism.

Another method of growing microbes on solid media is to pour some sterile medium into a Petri dish. After it has solidified, the material to be examined — milk, for example — is gently streaked over the surface in three or four parallel lines. Colonies

develop after proper incubation. These may be fished and subcultured.

Still another method of growing pure cultures of bacteria is to incline a tube of agar medium while hot, so that when it solidifies it forms a slanting surface, on which each organism grows in characteristic fashion. (See fig. 34.)

Petri dishes do not fit so tightly but that they permit the access of air. Certain microbes, however, called anaerobes, grow

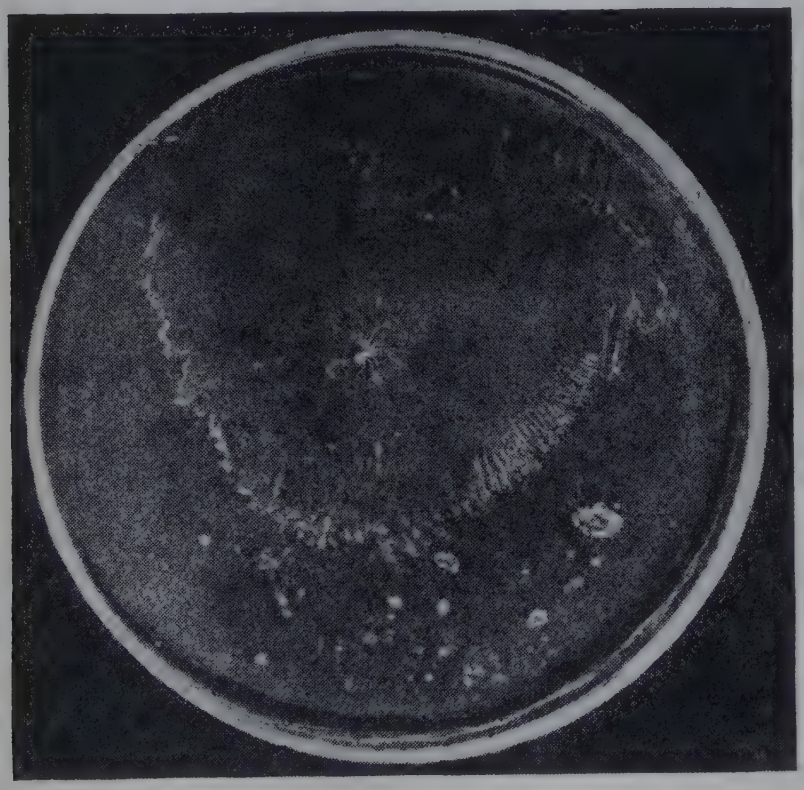


FIGURE 33

Colonies of bacteria on an agar plate (Petri dish). (After Conn and Conn.)

FIGURE 34

An "Agar Slant" for growing microbes on a solid medium in a test-tube. (After Conn and Conn.)

best in the absence of free oxygen. Consequently, for these the Petri dish must be placed in a receptacle from which oxygen has been removed or replaced by some other inert gas, such as hydrogen or nitrogen. (See fig. 35.) Various other ingenious methods have been devised for excluding free oxygen while growing bacteria in test-tubes. For this purpose chemicals, oil, vaseline, or bits of animal tissue have been employed. Thus a layer of sterile vaseline above the liquid medium prevents air from entering the medium. If the medium is boiled just before adding the layer of vaseline (which is added as a warm liquid and solidifies on

cooling), then the free oxygen originally present is driven off by heat, and the vaseline seal prevents any further access of this gas.

Finally mention should be made of a method for isolating single living microbes in fluid media. By means of a very finely drawn-out capillary glass tube in the Chambers apparatus, absolutely pure cultures may be made by fishing single cells under the microscope.

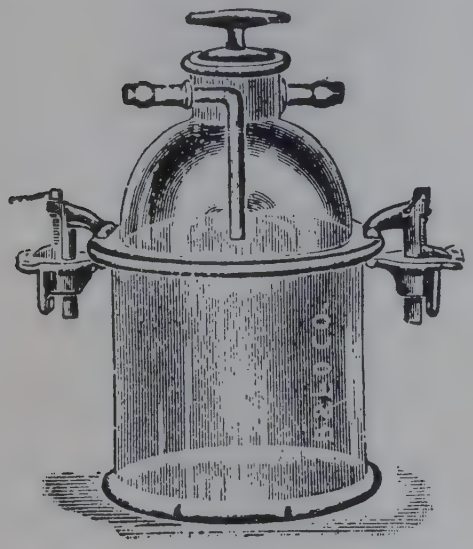


FIGURE 35

Jar from which air is exhausted so that bacteria may be grown anærobically on agar plates. (After Park, Williams, and Krumwiede.)

The counting of the actual number of microbes in any given substance is a difficult matter. Assuredly, the mediæval problem of determining the number of angels which could stand on the point of a needle seems only slightly more baffling. How, for example, is the number of microbes in a quart of milk determined?

Lister in 1877 pointed the way by introducing the dilution method. The principle is a simple one. A million microbes from a drop of milk are patently too many to count on a Petri dish — between fifty and one hundred is a reasonable number. Consequently, it is necessary to reduce the larger to the smaller number by dilution, which is readily done in definite proportion by the addition of fluid.[1] The same procedure may be applied to water analysis, food analysis,

[1] Take a representative amount of the milk, say one ounce (which is 1/32 of the total). Dilute this ounce of milk by adding nine ounces of sterile water (or, better, sterile physiological saline, which is water to which table salt has been added in the same proportion as the salts present in the human body-fluids — namely, 0.85 per cent). Agitate well this "1 to 10" dilution (one ounce of milk plus nine ounces of milk is one-tenth of ten ounces, so that the original ounce of milk is one-tenth of the present volume). To one part of the "1 to 10" dilution add nine parts of sterile saline, making a "1 to 100" dilution, because the original ounce of milk has been diluted ten times and again ten times, or one hundred times in all. By the same dilution process dilutions running 1 to 1,000,000 or more may be easily made. "Plate out" the "1 to 1,000,000" dilution by adding broth agar to it and pouring it into a Petri dish. After incubation ten colonies, let us say, appear. Since the dilution is 1 to 1,000,000 there must be ten times a million microbes in the original ounce of milk, or ten million microbes present. If there are ten million microbes in one ounce of milk, and there are thirty-two ounces of milk in one quart, there must be thirty-two times ten million microbes in the quart of milk, or 320,000,000 microbes in all.

etc., to obtain the number of microbes present in any material under investigation. Special counting-chambers have been devised for making direct counts under the microscope after the proper dilutions have been made, but these are not so accurate as "plating out" in Petri dishes.

3. ANIMAL EXPERIMENTATION

The antivivisectionists have yet to persecute the bacteriologist for what he does to microbes. But they do hamper him in his experimentation with animals. It is hard to believe that in this scientific era there can exist a group of individuals who not only wilfully shut their eyes to the benefits which animal experimentation has conferred on the human race (who willy-nilly profit by it), yet who impede further progress on nothing more than sentimental grounds.

The scientist makes pets of his animals, he cares for them jealously. His laboratory is anything but a howling menagerie and it reeks more of anæsthetics than of curses or cruelty. Fussy old ladies make much ado over the horrors perpetrated on helpless animals by the scientist's scalpel. But animals are not subjected to painful operations without the use of anæsthetics. One significant fact usually overlooked by the antivivisectionist is that, regardless of man's moral right to utilize animals for the prevention and treatment of human disease, he has at any rate done much for the prevention and treatment of animal diseases.

White mice, white rats, guinea-pigs, and rabbits are the universally familiar laboratory animals. They may be inoculated in many ways: rubbing or injecting infectious material into the skin; injecting it below the skin, into the veins, or into the body cavities; inhaling and even swallowing it. But none of these methods are more painful than the bite of a mosquito. Often inoculation into an animal is the final test in determining the cause of a particular disease, such as tuberculosis.

It will be remembered that it was Koch who really made of bacteriology an exact science. He not only established the causal relation between microbes and human disease, but paved the way for his colleagues to discover the germs causing diphtheria, typhoid fever, and other infectious diseases. In those days it was

not unusual for an investigator to find an unfamiliar microbe in a certain disease and jump to the conclusion that it was the cause of that disease. To guard against such hasty and erroneous conclusions the great scientist laid down what are known today as "Koch's postulates" — namely:

(1) A specific microbe must always be present in the disease.

(2) It should be isolated in pure culture from the diseased body.

(3) When the pure culture is inoculated into suitable animals, it should reproduce the same disease process.

(4) It should be recovered in pure culture from the experimental animal.

Animals, therefore, serve an important purpose in the bacteriologic laboratory in the study of disease. They are sometimes utilized to perpetuate certain microbes which would lose their characteristic properties if grown upon artificial media. Finally, animals are indispensable in the mass production of antitoxins and serums used in the treatment of diphtheria and other diseases, as will be recounted more fully later.

Microscopic methods, artificial cultivation, and animal experimentation represent man's weapons in his fight against the microbial universe. To be sure, there are death-dealing microbes which evade the most skilful search; but human thought, ingenuity, and perseverance will eventually result in victory.

Chapter IV

WHAT MICROBES DO

To the query: "What do microbes do?" the commonplace response would be: "Make trouble." But that would cover only one phase of their activity. We have seen that microbes are as much the creatures of their environment as are any other of the earth's inhabitants. They have definite requirements with regard to food, temperature, moisture, oxygen, and light, all of which modify their properties. But, as Jordan states, "they are not . . . mere passive victims of their environment. The influence exerted by the higher forms of life upon surrounding objects is often impressive, and bacteria also can react upon their environment in a direct and sometimes surprising fashion. Relatively slight physical and chemical changes in bacterial surroundings may give rise to a remarkable and profound disturbance of the surroundings themselves. The rapid invasion of the animal body by bacteria and the resultant putrefactive change which takes place soon after death is a familiar instance. The infection of the body of the fowl by the anthrax bacillus, which has no effect upon the normal animal, but gains a foothold and effects injury when the temperature of the fowl is lowered only a few degrees below the normal, affords another example."

Consider the effects of microbial growth. The physical effects, strange though they may seem, include the production of heat and light. Not, of course, on any commercial scale. But where decomposition is proceeding at a rapid rate, heat is likely to be evolved. Thus the heating of manure piles or damp hay, which often actually results in an outbreak of fire, is a familiar farmyard occurrence starting from microbial activity. Likewise the storing of tobacco in a moist condition induces a fermentation process which evolves heat. As for light-producing bacteria, have you never noticed the phosphorescence upon decaying fish or meat? Further, the luminescence or phosphorescence of living marine animals is often caused by bacteria.

The chemical products of microbial growth are as complex as those of human growth. In microbes, as in man, they may take the form of: secretions, which are either held by the microbial cell or liberated; excretions, or waste products; disintegration products, formed by the breaking down of nutrient substances attacked by microbes; or the dead microbial cell itself — that is, all the salt and chemical constituents which compose the contents of the microbe (as pointed out by Jordan).

The most important secretions of microbes are the ferments or enzymes. The fermentation of sugar into alcohol is a characteristic activity of yeasts, a phenomenon described in the early days of bacteriology by Schwann and Pasteur. Such fermentation is brought about through the agency of an enzyme secreted by the yeast cells. All living cells, human or microbial, contain enzymes, which are substances having the power to bring about chemical changes without actually entering into the reactions they induce. Enzymes are specific; thus the enzyme zymase, which breaks sugar down into alcohol and carbon dioxide, can do only that and differs therefore from lactase, which only splits milk sugar into lactic acid. There are a great number of different enzymes and they are variously distributed among the microbes. Some microbes secrete few enzymes, others many. Enzymes take their name from the substances they attack and are therefore characterized as sugar-splitting enzymes (zymase, lactase, maltase, invertase, etc.); proteolytic enzymes (pepsin, trypsin), which attack proteins and are found in the human intestinal tract; diastatic enzymes, converting starches to sugars, present in human saliva; fat-splitting enzymes (lipase), etc. The chemical effects produced by microbial or human enzymes are obviously manifold.

To say that putrefaction, decay, and fermentation are caused by microbes fails to bring out the important fact that it is the enzymes of microbes which are really responsible for these important natural processes. Putrefaction, as has been stated, is the decomposition of animal or vegetable matter by bacteria which do not require free oxygen (anaerobes); decay is decomposition by bacteria in the presence of free oxygen (aerobes). Some bacteriologists, however, prefer to define these terms, not on the basis of the oxygen requirement of bacteria, but rather on the

basis of the composition of the substances attacked. Thus, putrefaction is regarded as the decomposition of substances containing nitrogen, such as animal tissue or albumen; decay or fermentation is the decomposition of vegetable materials, chiefly carbohydrate in nature. This distinction, to put it another way, hinges, on the one hand, upon the activity of proteolytic enzymes, which decompose nitrogenous materials; and, on the other hand, upon the activity of sugar-splitting and diastatic enzymes, which decompose carbohydrates. The decomposition of carbohydrates by enzymes may in turn result in the formation of acids, such as lactic acid from milk; and gases, such as carbon dioxide.

Putrefying meats or fish may yield ptomaines, which are definite chemical substances. "Ptomaine poisoning" is a popular misnomer. "Ptomaine" comes from the Greek, meaning "a dead body," and refers only to poisonous products of bacterial growth — not to any or all poisons to be found in food.

Many bacteria have the power of decomposing or reducing substances containing sulphur (present in most proteins) to hydrogen sulphide, a foul-smelling gas which has the characteristic odour of rotten eggs, only too familiar to the frequenters of sulphur-spring resorts. Some bacteria also reduce nitrates to more elementary substances. These processes will be discussed later, together with the building up of nitrogen compounds by bacteria.

One of the most striking properties of microbes is their capacity to produce various pigments. The production of colours by many bacteria when grown on suitable media is a very complex and fascinating study. The pigments best known are red, yellow, orange, green, violet, blue, and fluorescent. While bacterial pigments vary considerably in their chemical composition, they have been classified among the large group of pigments called lipochromes, which are found alike in animals and vegetables. Common examples of non-bacterial pigments are to be found in such coloured edibles as egg-yolk, carrots, fat, etc. The most familiar bacterial pigments are perhaps the vivid orange and yellow of the pus-forming staphylococci, visible when a pimple breaks. It is a curious fact that unfavourable environmental conditions of temperature and moisture diminish or totally inhibit the power of bacteria to produce pigment.

The vital capacities of microbes, though very briefly sketched

here, are nevertheless of tremendous significance. Microbes are the intermediaries between the animal and vegetable kingdoms. Animals could not exist in a plantless world, for they require organic (carbon-containing) matter, which can only be derived from plants. Unlike animals, plants are able to manufacture organic compounds from such a simple source as the carbon dioxide of the atmosphere. This is accomplished in the presence of sunlight by means of chlorophyll, the green colouring-matter of plants. Complex organic compounds are built up in plants out of the carbon dioxide in combination with water and the various salts which plants absorb from the soil. Animals then satisfy their requirements for organic compounds by ingesting plants.

Plants manufacture food for animals; but animals go to some effort to return the compliment. After an animal has digested plant material, it excretes the unutilizable residue, which is naturally simpler in composition than the food was before swallowing. This residue, however, is not ordinarily simple enough to serve directly as a source of food for plants. This is the point at which microbes become so important. They break down animal excreta. But they do more. They destroy dead plants and animals. It staggers the imagination to conceive a world in which all plants and animals would persist in their original form after death. The world would be so cluttered that all other life would become impossible. Thanks to the microbes, dead plants and animals are gradually destroyed, returning to the earth from whence they sprang, to furnish food for growing plants, to pass through animals, and to be reduced again by microbes to inorganic salts. The two great forces of construction and destruction, rotate the wheel of life. Matter is never destroyed — it merely undergoes continuous change. All living things grow and decay and make food for other organisms. Destruction lays the foundation for construction.

Chapter V

MICROBIAL ATTACK AND MAN'S RESISTANCE

It is difficult for man to reconcile himself to disease. Much of his time and effort has been spent in determining why his body should be chosen as the victim of such an unwelcome visitation. According to the earliest explanation of disease, the body was possessed by an evil spirit. The demon selected a favourite site for his throne and ruled mercilessly.

Even today such beliefs are encountered among savage tribes living in a primitive state, a state which constitutes the heritage of twentieth-century man. Mankind suffered through many centuries before disease was defined in terms of flesh and blood. And many more centuries passed before man gained a thorough knowledge of the structure and the function of the human body. The theories to account for the origin of disease have been many and ingenious. Hippocrates, "the father of medicine," taught in 420 B.C. that the body contained four humours: blood, phlegm, yellow bile, and black bile, which in the proper balance maintained health. When the balance was destroyed, illness ensued. The credibility of this theory was never vigorously attacked until the seventeenth century. Then came a period of frenzied theorizing about the origin of disease, during which time there were as many schools as there were enthusiasts. Disease was regarded as "an intestine movement of particles"; a struggle between nature and disease-producing matter; a lack of tone; or an insufficiency of stimulus. While homœopathy, one of the most enduring of these credos, in treating disease conditions with minute doses of drugs, did little harm, the psychic effects were so salubrious that its founder, Hahnemann, died (in Paris in 1843) a millionaire. And his spiritual descendants still collect.

The maelstrom of confused theory was finally directed into a definite current. Louis Pasteur rose like a Triton. By the brilliance of his genius, by the clearness and breadth of his vision, he

formulated the bacterial or germ theory of infectious diseases, which must for ever dominate medicine. No longer could malevolent spirits be held responsible for disease, nor could an improper admixture of the four humours be regarded as the cause of ill health. Disease was a struggle for existence between men and microbes. It was life preying on life; the invasion of the *macro*-organism by the *micro*-organism.

When micro-organisms enter human or animal tissues there to remain and multiply, infection occurs. Not only are microbes the universal inhabitants of our environment, but they inhabit our bodies as well. They swarm in the body cavities, the mouth, the nose, the female genitalia, as well as in the respiratory and intestinal tracts. The skin teems with microbes. In each part of the body certain types of microbes generally, though not invariably, occur. Thus staphylococci are found on the skin, colon bacilli in the intestines, and Döderlein's bacillus in the vagina. Many harmless microbes, the saprophytes, inhabit the body along with the other microbes, the parasites, capable of producing disease.

Indeed, microbes capable of causing disease are not always able to exercise that function. For example, staphylococci on the surface of the skin are innocuous, but once the skin is broken, they become active, forming pus. In other words, the mere association or contact of man with microbes does not inevitably result in infection — there are other important considerations. First and foremost, infection takes place only when micro-organisms gain entrance into the bodily tissues and *multiply*. This is not to say that when a few bacteria alight on some part of the human anatomy, forthwith disease sets in. Happily such is not the case, for the body has weapons to dispose of such invaders. It is when disease-producing microbes are present in large numbers, or when bodily resistance proves inadequate, that microbes force an entrance and multiply.

This problem of bacteria attacking the human body is the fulcrum upon which is balanced the biological struggle for existence between man and microbes. From our present meagre store of knowledge, the odds seem about equal. Our microscopic adversaries have the fairy-tale advantage of being neither seen nor heard. We, the macroscopic army, have our mystifying creations

of science: the microscope, the myriad antiseptics, and the subtle skill by which we use the very products of these organisms, even their own dead bodies, to destroy them.

Many factors predispose man to infection or endow him with resistance.[1] When virulence exceeds resistance, infection occurs; when resistance exceeds virulence, infection does not take place. But neither the virulence of the bacteria nor the resistance of man is an absolute term: each depends upon a number of factors. From the outset we are equipped with certain defences against bacterial invasion. From the point of view of the microbes which hover about us seeking opportunities for invasion, there is first the unbroken skin. This presents perhaps the most resistive barrier. It offers a mechanical resistance because the surface layer of cells is so thick that none of the bacteria, such as the staphylococci which are normally found on the skin, can penetrate deeply into the tissues. Infection occurs but rarely through the ducts of sweat-glands or hair follicles. Any wound or abrasion, on the contrary, is an open door with a "Welcome" sign on it, which is not long ignored. Even then there are secondary defences. Under the surface of the skin itself there are layers of connective tissue which bar the way to farther invasion by microbes.

Compared with the skin, the mucous membranes which line the mouth, nose, eye, and intestinal tract are much less impassable. They might, indeed, be considered to invite bacterial multiplication because of their moisture and warmth. True, mucus has a slight germicidal effect, but not sufficient to prevent the bacteria from over-colonizing these regions *if they are allowed to remain*. A constant flow of mucus keeps them moving too rapidly to do much damage. The eye is presided over by the faithful eyelashes and eyelids, which keep intruders at bay. And even tears serve more than one purpose: they wash away the irritating foreign intruders. Further, the tortuous nature of the nasal passages makes for considerable resistance to the entrance of dust and bacteria. This is augmented by nasal hairs, which always point in an outward direction.

It is in the mouth, that dark, dank, warm chamber, that the

[1] Infection (I) may be represented by the ratio: virulence (V) of microbes over resistance (R). $(I = \frac{V}{R}.)$

bacteria really feel at home. If a bacterial census of the mouth were taken, more than fifty different varieties might be counted. But even here their residence is only temporary, since saliva acts as a wash.

Many of these mouth bacteria are washed into the stomach. Here they cannot stand the acid test. It has frequently been demonstrated that the gastric juice contains enough acid to kill practically all the bacteria which find their way into the normal stomach. The famous bacteriologist Koch, in experimenting with animals, found it necessary to neutralize the acidity of the gastric juice before he could persuade the bacteria to multiply. The intestinal secretions, on the other hand, have a comparatively feeble antiseptic power. Nevertheless, the bile from the liver is said to have some germicidal properties.

In brief, then, it may be said that our bodily defences against bacteria are none too potent. A few mechanical barriers, a few chemical bulwarks, are all that stand between us and the invading horde. All the more important, therefore, to keep our defences functioning at their maximum efficiency.

We enter this world armed with some weapons and burdened with many weaknesses. The predisposition to many diseases is specific, or in the species. Thus, of all members of the animal kingdom, in *homo sapiens* alone does syphilis occur. Similarly with gonorrhœa, influenza, diphtheria, Asiatic cholera, typhoid fever, leprosy, scarlet fever, smallpox, measles, typhus fever, yellow fever, and poliomyelitis. Many of these diseases may be produced experimentally in animals, but they are not developed in the natural course of events. On the other hand, there are many diseases to which animals are susceptible which fortunately do not attack man. Among these the farmer knows only too well the ravages of chicken cholera and cattle-plague. Even our friend the dog has his own peculiar distemper.

Sociologically all men may be created free and equal. Biologically they are not. All men are not equally susceptible to the diseases which affect the species, for within this broad category racial differences occur. The American physician is familiar with the conspicuous predisposition of the Negro to tuberculosis. Eskimos and American Indians are similarly prone to the "white plague." The Caucasian, on the other hand, succumbs readily to

yellow fever, from which the Negro is comparatively immune. In discussing racial differences of this character the importance of personal and social hygiene can scarcely be overlooked.

Familial susceptibility to infection is frequently very striking. Anyone can count within his immediate circle families several members of which have been victims of the same disease. In many instances this may be due to the infectious nature of the disease, but when members of the same family through successive generations contract scarlet fever, tuberculosis, or rheumatism, then it may be inferred that it is a predisposition to the disease rather than the infection itself which has been transmitted. Strictly speaking, no microbial disease is hereditary — contrary to popular belief, which confuses congenitally acquired diseases, such as syphilis, with heritable characters transmitted only in the germ-plasm.

Conspicuous variations exist in individual susceptibility to infection. The many factors which determine individual susceptibility are very complex. Who has determined the why and wherefore of the common cold? Your proverbial berubbered, umbrella'd, fussy old gentleman is not infrequently the one who sneezes the loudest. Bacteria are so mobilized as to attack every age. "Children's diseases," such as scarlet fever, whooping-cough, or measles, are rarely known to affect adults. Pneumonia, so fatal to adults, can boast little mortality among adolescents, but again is highly dangerous to babies. To a degree, sex may also condition susceptibility, in that there are certain diseases which are peculiar to each sex because of anatomical differences.

Individual susceptibility is easily demonstrated in epidemics. For example, in a typhoid-fever epidemic where the disease is spread through the agency of an infected water- or milk-supply and everyone is equally exposed, not everyone contracts the disease, and even the victims are not affected to the same degree. The man who is in the pink of condition need have little concern for the disease-producing bacteria with which he comes in contact. Let him become run down and he becomes thereby an easy prey to pneumonia, tuberculosis, and the like.

Species, racial, familial, and individual variations are the biological factors constituting inherited susceptibility and immunity. But immunity may also be acquired. It is well known that

certain of the infectious diseases are contracted only once in the lifetime of an individual. A single attack of typhoid or yellow fever develops resistance to the germ in such a way that subsequent exposure is harmless, for immunity has been established.

It is generally believed that excessive fatigue predisposes to infection. Normal white rats are highly resistive to anthrax, the dreaded disease which lurks in improperly sterilized brushes. When these animals are exhausted by overwork in a treadmill, they lose their resistance and can be infected with anthrax. Similarly, we know that hard labour, mental or physical, which involves late hours and inadequate periods of rest and recreation, especially when associated with inadequate nutrition and foul air, may lower a person's resistance so that he is likely to succumb to tuberculosis, typhoid fever, pneumonia, or similar diseases.

Although a single attack of certain diseases confers immunity from subsequent attacks, it should nevertheless be recognized that frequently previous infection with the same or another infectious disease may induce a tendency to renewed or secondary infection; chief among such diseases may be mentioned erysipelas, acute rheumatism, pneumonia, and influenza. Furthermore, a single attack of an infectious disease may increase susceptibility to other infectious diseases, notably tuberculosis.

Malnutrition increases susceptibility to infection. In past centuries Europe and Asia have been scourged by epidemics of plague, cholera, typhus and typhoid fevers following in the wake of devastating famine. The nature of the diet is of importance in determining susceptibility to infection, for it is well known that diseases to which carnivorous animals are susceptible usually do not affect herbivorous animals, and vice versa. Intoxications of various kinds must also be considered. It has been observed clinically that excessive indulgence in alcoholic beverages may predispose to infections such as pneumonia. In experiments with animals it has been found that the administration of intoxicants renders them more susceptible to infections.

Exposure to cold and dampness frequently lowers the resistance of men and warm-blooded animals. Pasteur found that fowls, which are naturally immune from anthrax, were readily infected if they were inoculated after their body temperature had been reduced by a cold bath. Curiously enough, the converse has

been proved by experiment. Gibier has shown that frogs, which are cold-blooded animals and are naturally immune from anthrax, are readily infected if their temperature is previously elevated and maintained at the temperature of the human body — 98.6°F.

Injury and morbid conditions in general may frequently pave the way to infection. Lungs which have suffered lesions due to pneumonia, as is well known, are particularly easy prey for the germ of tuberculosis. Similarly, diabetics often suffer from skin infections, boils, and the like.

It is apparent, therefore, that the nature and state of the individual are important in determining the occurrence of infection. The conditions influencing the infecting agent itself are likewise of great importance. Thus the *virulence* of a micro-organism — that is, its power of growing in the body and producing injury — is as variable as the susceptibility of man — and in our bland and social way, when infected, we call ourselves the hosts.

Bacteria, like human beings, are the slaves of their environment. In the presence of unfavourable conditions the activities of bacteria are diminished, their virulence is attenuated, and they no longer possess the power to induce disease. Just as man's resistance is lowered when exposed to extremes of temperature, so the bacteria subjected to radical changes in temperature or moisture become weak to the point of extinction. Similarly, poisons serve to reduce their virulence. Sunlight, which is so beneficial to man, annihilates them. Furthermore, the actual production of infection depends to a considerable extent on the number of bacteria introduced into the body. Frequently, one may successfully dispose of a few influenza bacilli without contracting the disease, while the advent of a large number will result in untoward consequences.

It is interesting to note, also, that some kinds of bacteria seem to have a special affinity for certain organs of the body. Rosenow has made much of this in his work on focal infection, which will be discussed presently. Besredka and Plotz have made significant contributions to the doctrine of local immunization. They claim that certain microbes attack certain tissues, and if those local tissues are artificially immunized, infection does not occur. Thus the typhoid-fever bacilli attack the intestinal tract

but do not infect the skin; and anthrax bacilli attack the skin, but if swallowed, cause no infection of the intestinal tract.

How do microbes cause disease? By means of the poisons or toxins they produce. Some bacteria throw off or excrete toxins called "extracellular" or "soluble" toxins. Diphtheria and tetanus (lockjaw) bacilli belong to this category. Other bacteria, such as cholera-producing vibriones, retain toxins within the cells themselves and are therefore known as endotoxins. Finally, there are toxic split-products or intermediate products of microbial decomposition, among which must be considered the ptomaines, previously mentioned.

Infection is a tug of war between the individual on the one hand and the invading microbes on the other. Both adversaries depend upon many various factors to best fit them for the struggle. Occasionally a temporary advantage is gained only to be finally relinquished. Defeat means death. Science has done much to condition us for the struggle, yet there remains much knowledge to be gained.

Infection in another sense has recently achieved notoriety. The doctrine of focal infection [1] compels the attention of the physician and the layman. It has been shown in many instances that certain bodily organs may harbour bacteria which occasion no immediate pain, but which cause grave general maladies. Infection in any part of the body, often suspected and difficult to ascertain, has been considered responsible for such systemic diseases as acute or chronic rheumatism and heart-disease. Hence the fad of removing teeth, tonsils, and various integral portions of the human anatomy, a fad which rests on a scientific basis which is none too secure.

All individuals manifestly do not possess the same degree of resistance to harmful bacteria. When the body is invaded by these bacteria, the natural defences are actually increased by their presence in the blood. Thus, in response to some infections — as, for example, boils — there is an accumulation of white corpuscles, which not only protect against further invasion, but actually kill off the invaders, as described by Metchnikoff under

[1] A complete discussion of the material of this chapter may be found in the author's *Why Infections?* (New York, Alfred A. Knopf, Inc., 1926), which is here epitomized.

the term "phagocytosis." He found that the introduction of foreign bodies, such as bacteria, into the tissues causes myriads of white corpuscles to leave the blood-stream and mobilize themselves for the fray. This fighting white army surrounds the invaders and, if sufficiently great, devours them, forming pus. If the bacteria outnumber the white army, however, the host succumbs. Phagocytosis may be intensified or diminished in a number of ways. Thus certain substances called "opsonins" (from the Greek meaning: "I cater for, prepare food for") present in the blood-serum act on the bacteria in such a manner as to make them more readily digestible by phagocytes.

In response to other infections, such as typhoid or diphtheria, the body further elaborates specific combating substances. These are known as "protective antibodies" and are the basis for vaccination, which will be discussed in a later chapter. Other substances formed in the animal body after the introduction of bacteria or their products are agglutinins, which cause bacteria to clump or agglutinate: and precipitins, which provoke the precipitation of bacteria.

Man needs all the resources at his command to resist the invasion by his microscopic adversaries — in a word, to gain immunity. Immunity, as we have seen, is a difficult concept to analyse, for there are in reality different kinds of immunity — racial, species, familial, and individual. There is, further, natural immunity as distinct from acquired immunity. Natural immunity is individual resistance to disease, which is a birth endowment. Thus, a certain number of individuals, without taking any special medical precautions, never contract pneumonia; they resist the disease by virtue of their natural immunity.

Immunity may be acquired either through recovery from such an infectious disease as measles; or artificially. Again, artificial immunity may be either active or passive. In active immunity the body is directly stimulated to fight the invading microbes. In the treatment of hydrophobia (rabies) increasing doses of the virus fortify resistance to such an extent that the otherwise fatal bite of the mad dog is rendered innocuous. Another common example of this type of immunity is vaccination against smallpox. The latter consists in introducing a small amount of cowpox virus, which so stimulates resistance that the body is not infected

upon exposure to smallpox. Passive immunity, on the other hand, requires no added effort, for it is an immunity which is conferred by the administration of protective substances, as in diphtheria antitoxin. Injection of diphtheria antitoxin, which contains antibodies against this specific disease, takes care of the toxin or poison generated by the diphtheria bacillus. The body is thus the battle-field upon which the fight is waged between toxin and antitoxin.

There is no rule of thumb whereby one can obtain immunity against microbes. Each microbe must be guarded against in a specific manner. The disease-producing power of the microbe is as variable an entity as the resistance of the individual; both are extremely complex in character. What are these microbes which beset us? Let us call the roll.

Chapter VI

DISEASE-PRODUCING COCCI

I. PUS-FORMERS, SCARLET FEVER, AND ERYSIPELAS

Pus-formation is a familiar phenomenon. The thick yellowish-white secretion of inflamed tissues, known as "pus," consists chiefly of modified white blood cells in a creamy fluid. Pimples, abscesses, carbuncles, boils, or furuncles contain pus.[1]

Pus-forming bacteria are found widely distributed in nature. While many kinds of bacteria can form pus, the principal species,

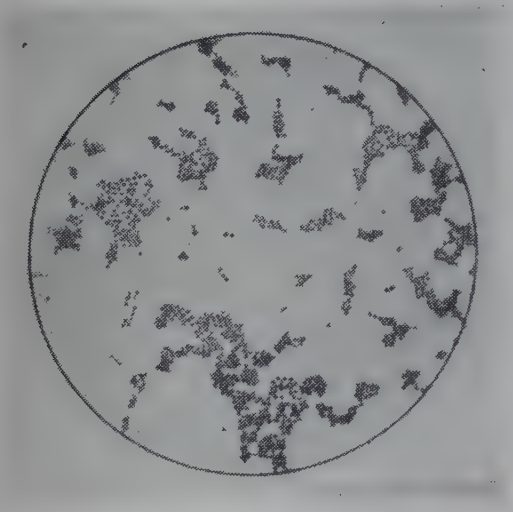


FIGURE 36

Staphylococcus aureus (magnified 1000 times). (After Jordan.)

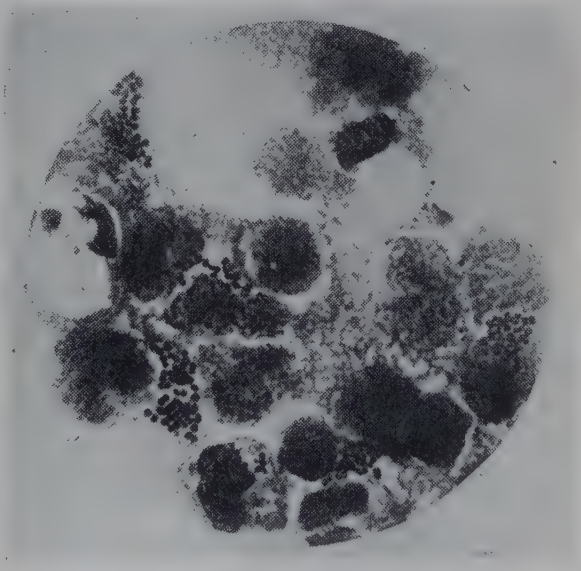


FIGURE 37

Staphylococcus aureus amid pus cells. (After Jordan.)

in the main, belong to the well-known group of spherical microorganisms called "pyogenic" (pus-forming) cocci or micrococci. Chief among these are the staphylococci and streptococci. (See figs. 36, 37.) As a rule, man is more susceptible than animals to infection by staphylococci. Rabbits and white mice, however,

[1] Pus has been defined as "destroyed tissue broken up into its constituent elements. Emigration of colorless blood corpuscles certainly participates in the formation of pus and in the purulent discharge of proud flesh or granulation tissue which forms after the discharge of pus from the abscess and is probably the main source of pus" (Atkinson in *Journal* of the American Medical Association, XIII [1889], 374).

are rather easily infected. A staphylococcus infection in man commonly appears as a boil (furuncle) or abscess. Since staphylococci are ever present on the surface of the skin, it requires only a scratch or an abrasion for them to gain a foothold. It is likewise possible that they may be rubbed into the roots of the hair or pores of the skin. "Opportunists," Kendall aptly calls them.[1]

Boils are painful. Consequently there is a temptation to open them before they have come to a head. But if this is done too soon, the infection spreads, causing a still more painful carbuncle or even blood-poisoning, particularly if the boil happens to be located about the nose or lips. No man likes to walk around town with his head inclined at a flirtatious angle and a large pad of gauze sticking out of the back of his collar. And it is questionable whether ladies with boils better concealed are any more comfortable or less embarrassed.

Staphylococci

Staphylococci may choose any part of the body in which to produce abscesses. These in turn may lead to blood-poisoning characterized by fever, chills, malaise, etc., or to focal infections, which will be discussed presently. Staphylococci also cause a very contagious skin-disease called "*impetigo contagiosa*," which runs riot through children's wards or dormitories. Pus-formation in bones (osteomyelitis) often occurs after fractures, as a result of the invasion of staphylococci. When they get into the brain or spinal-cord membranes, meningitis may ensue.

All persons are not equally susceptible to infection by the same microbes. The staphylococcus flourishes when general resistance is lowered, as in run-down conditions, malnutrition, and constitutional diseases such as diabetes. On the other hand, college crews are notoriously prone to outbreaks of boils.

Just why such embarrassing sites as the back of the neck and the buttocks are selected by the staphylococci set on developing furuncles and carbuncles may appear something of a mystery. The unbroken skin, it has been said, resists bacteria, but when the skin is abraded, it is then an easy matter for them to gain entrance. A collar always rubs against the back of a man's neck.

[1] A. I. Kendall: *Bacteriology, General, Pathological and Intestinal.* Philadelphia, Lea and Febiger, 1928.

This irritation breaks the skin sufficiently to give bacteria their start. In this connexion it is interesting to observe that since men have taken to wearing more soft collars, the incidence of boils on the back of the neck has been less than in the days of the heavily starched stiff collar. Again, the fact that men wear collars explains why they suffer from boils on their necks much more frequently than do women. Similarly, the outbreaks of boils in college crews may be traced back to the continued friction of the sliding seat and the wearing of apparel which has become saturated with perspiration. A daily change of trousers and sweatshirt would go far in eliminating outbreaks of boils in our strenuous young athletes. Boils are also common in mechanics, particularly those who work in garages. The grease with which their arms are coated tends to bottle up the staphylococci and give rise to infection.

"Once a victim of a staphylococcus infection, often a victim," seems to be the rule, for a single attack apparently induces a susceptibility to further attacks.

The most familiar of the staphylococci is *Staphylococcus aureus*, which derives its name from the fact that it occurs in grape-like clusters (*staphylo*) of spheres (*cocci*), which produce a golden colour (*aureus*). It was first obtained from pus by Pasteur in 1880 and soon afterwards other investigators demonstrated that it actually causes pimples, abscesses, and other similar conditions. This staphylococcus is readily stained by the common bacteriologic dyes and is Gram-positive. (See page 45.) It is non-motile, since it possesses no organs of motility; it does not have the power to form spores; it grows best in the presence of free oxygen and hence belongs to the aerobes; but it can also live in the absence of free oxygen and is therefore also a facultative anaerobe; and finally it flourishes on all the ordinary laboratory media.[1] When grown on solid media (containing agar or gelatin), *Staphylococcus aureus* produces the characteristic rich golden yellow colour which gives it its name. It ferments sugars with the production of acids (lactic, butyric, etc.), which, it has been maintained, play a rôle in the production of pus.

Although staphylococci do not produce spores (which tide

[1] Unless otherwise stated, all bacteria to be described have the same properties as regards motility, oxygen, and spore-formation.

bacteria over environmental adversities), nevertheless they are characterized by a great capacity of resisting heat, cold, drying, direct sunlight, or chemical disinfectants. In fact, they are considered to be among the most hardy of non-spore-bearing bacteria. Thus staphylococci may remain alive for weeks and months in pus which has dried upon silk, cloth or paper. The reason why staphylococci are so dangerous to man is that they produce poisonous substances which attack white blood corpuscles and which dissolve red blood cells. (They also produce an enzyme, gelatinase, which liquefies gelatin.) Staphylococcus infections are easily acquired. The best method for combating boils and abscesses is not by eating yeast, although on occasion this has been helpful, but through the injection of killed staphylococci prepared as a vaccine. Serums and leucocyte extracts have been made which are also said to protect against the ravages of these microbes.

Different strains of staphylococci are differentiated by the colours they produce, which range from white through golden yellow, to pale brown. Upon this basis of pigment production *Staphylococcus albus* and *Staphylococcus citreus* earn their names; the former yielding white colonies; the latter, lemon-yellow colonies. They resemble the golden orange *Staphylococcus aureus* in form, character, and all other particulars except that their pus-forming properties are not so markedly developed. Other pus-formers are *Micrococcus tetragenus* which occurs in tetrads (that is, groups of four cocci), to be found in tubercular sputum; and *Enterococcus*, a rather oval-shaped coccus frequently encountered in the intestinal tract of infants and adults, usually without any particular significance as regards intestinal disease.

Streptococci

Streptococci are more important in producing infection of a primary or secondary nature than any other single group of disease-producing microbes, according to most authorities. In multiplying, these spherical microbes divide in a single plane to form chains (hence the name: *strepto* = chain), unlike the grape-clustered staphylococcus previously described. (See fig. 38.) This distinction was noted by Pasteur. There are so many different kinds of streptococci that it is almost impossible to classify them

satisfactorily. In general they are divided into two categories: those which dissolve red blood cells and are therefore called *Streptococcus hæmolyticus;* and those which do not dissolve red blood cells, but produce a green colour on solid media containing blood, called *Streptococcus viridans* (*virid* = green).[1]

Of the disease-producing streptococci, the types which dissolve red blood cells (hæmolytic) are obviously most dangerous in causing general blood-poisoning and blood-poisoning following childbirth, abortions, etc. Throat inflammations, tonsillitis, pneumonia, and kindred pus-forming activities are not infrequently the result of the hæmolytic streptococci, which are often natural inhabitants of the mouth. Sore-throat epidemics have been traced to milk-borne streptococci. Massachusetts has had several such epidemics, one of the most recent of which occurred in the summer of 1928. Scarlet fever, erysipelas, and perhaps measles are caused by these micro-organisms. Furthermore, they are frequently found as secondary invaders in influenza, diphtheria, measles, and other diseases with serious, if not fatal, consequences.

FIGURE 38

Streptococcus pyogenes (magnified 1000 times). (After Conn and Conn.)

The streptococci which do not dissolve red blood cells (*Streptococcus viridans*) are most important in focal infections, causing acute and chronic general disease, such as subacute bacterial endocarditis, which is an infection of the heart valves.[2] Whether or not, as Rosenow and others contend, *Streptococcus viridans* is the cause of many general or systemic diseases, such as rheumatic fever, infantile paralysis, kidney and gall-bladder infections, the fact remains that so-called foci of infection revealing the presence

[1] Bergey's *Manual of Determinative Bacteriology* (Williams and Wilkins Co.) carries a new nomenclature of microbes which has not been followed in this volume because it has not yet been universally adopted. In both groups of streptococci will be found short-chain strains and long-chain strains, fermenters of one kind of sugar and fermenters of another kind of sugar. Much confusion attaches to the differentiation of the different strains. Suffice it to say that for the blood-dissolving *Streptococcus hæmolyticus* there are two principal types, one having a greater capacity than the other to dissolve red blood cells. The classification of streptococci called *Streptococcus viridans*, which do not dissolve red blood cells and produce only a green discoloration on blood-agar plates rests chiefly on their sugar-fermenting powers. Eight different types are described on this basis.

[2] See *Why Infections?*

of this micro-organism are of frequent occurrence and often difficult to find. The happy hunting-ground of these microbes is at the roots of the teeth, in the tonsils, in the mucous membranes which line the nose, eye, ear, intestinal tract, etc. Once localized, *Streptococcus viridans* pours its poisons into the blood-stream. But final proof that *Streptococcus viridans* is the specific cause of the long list of acute and chronic diseases is still wanting.

Scarlet Fever

It is hard to believe that scarlet fever was ever mistaken for measles. Yet it was before Sydenham, the great English physician of the seventeenth century, identified scarlet fever as the infectious disease now readily recognized all over the world.

Scarlet fever as a disease is no more severe than measles — in both infections it is the ensuing complications which are serious. Thus scarlet fever is probably the commonest forerunner of Bright's (kidney) disease in adult life. Also, a certain percentage of cases of organic heart-disease may be traced back to scarlet fever. One of the most frequent sequelæ of scarlet fever is middle-ear infection, the streptococci localizing at that point. Middle-ear infection is so common that many of our hospitals dealing with infectious diseases have a special service exclusively for mastoid and middle-ear infection.

Although adults are not exempt, scarlet fever is principally a children's disease, ninety per cent of fatal cases occurring among those less than ten years old. Young infants, however, rarely contract the disease. Where measles in a family of children would be likely to claim every member, susceptibility to scarlet fever is not so striking, so that perhaps only one or two become infected. However, familial susceptibility is evidenced by the fact that there are families in which several members succumb in rapid succession to the disease while other families remain uninfected. Compared with the white race, the black race is relatively immune from scarlet fever.

The disease is usually readily diagnosed. A seven-year-old child, for example, might be somewhat fretful and complain of a sore throat, but still continue to attend school. Even with a temperature of 102°F. (by mouth) the child is not particularly ill. But the papillæ (nipple-like processes) of the tongue stand out

and the tonsils are swollen, the entire throat being a bright raspberry-red. A bright red or "strawberry" rash is visible on the neck and extends downward over the entire trunk to the knees. It is most marked in the arm-pits and between the legs. The rash consists of characteristic red points. In short, this is an abbreviated description of a typical mild case of scarlet fever.[1]

The specific cause of scarlet fever was for a long time a perplexing bacteriologic problem. Many investigators have suggested that hæmolytic (blood-dissolving) streptococci were responsible for the disease. But it is only recently (1923–4) that this has been experimentally demonstrated by George F. and Gladys H. Dick of Chicago. Theirs is a perfect example of a carefully controlled scientific experiment. They resisted the temptation to jump to conclusions, and their results speak for themselves. One is reminded of the memorable experiments establishing that yellow fever is transmitted by the bite of a particular kind of mosquito (see chapter XVII).

With cultures prepared from the throat of a nurse who had contracted scarlet fever, the Dicks swabbed the throats of five volunteers. One developed a typical case of scarlet fever within forty-eight hours. Another had a sore throat and fever, but no rash. Three remained well. To make certain that the streptococcus and not something else in the culture had produced the disease, a control test was performed, by swabbing the throats of volunteers with a culture from which the living microbes had been filtered out. None of these volunteers became infected. Now for a crucial test — would these individuals succumb to an unfiltered culture — that is, one in which the streptococci were present? They did. One developed a typical attack of scarlet fever, while two developed sore throat and fever, but no rash.

Even this test did not establish an error-proof conclusion, because it was found that there were two types of hæmolytic streptococci associated with scarlet fever. One fermented mannite (a sugar), the other did not. The cultures used in the above experiments were of the mannite-fermenting type. Could the disease be produced by the other type? It is necessary to

[1] In this, as well as in the description of several other diseases, Morse's *Case Histories* has been very closely followed.

demonstrate that the causal organism is present in *every* instance of the disease in order to fulfil Koch's postulates (see page 54).

The Dicks therefore undertook the final experiment, utilizing a non-mannite-fermenting hæmolytic streptococcus isolated from the throat of a scarlet-fever patient. Two volunteers were chosen. One showed an entirely negative skin-test with the filtrate of the streptococcus previously used, indicating immunity from scarlet fever; the other showed a positive skin-test, indicating susceptibility to the disease. The tonsils of each were swabbed with the new culture. The volunteer who showed a negative skin-test remained well. She had no sore throat, no fever, and no rash. The volunteer who showed a positive skin-test, indicating a susceptibility to the disease, developed typical scarlet fever. The Dicks were therefore able to state that "since the streptococci used in these experiments have fulfilled all the requirements of Koch's laws, it may be concluded that they cause scarlet fever." Thus is the science of bacteriology advanced and medical history made.

Nor does it stop with the mere discovery of the causal micro-organism. There was still wanting a test to determine individual susceptibility to scarlet-fever infection, and, more important still, an adequate method for prevention and treatment. Russian bacteriologists had long since recognized that streptococci from scarlet fever produced toxins (poisons) when cultivated in broth. On this basis they produced serums and vaccines which yielded favourable results in their hands. But it was the Dicks again who devised a skin-test to determine individual susceptibility to scarlet fever, by means of an injection of toxin which is analogous to the more familiar Schick test for diphtheria (see page 96). Others, especially Park and the late Zingher, have carried out extensive investigations along the same lines. While it may be somewhat premature to make a final evaluation of the Dick test, the consensus of opinion is to the effect that it is a valuable criterion of susceptibility to scarlet fever.

Further, the Dicks have developed a toxin preparation which in proper dosage seems to immunize individuals who are found to be susceptible by the skin-test. Such immunity may last for a year and a half. Recently Larson suggested the use of a castor oil soap toxin preparation which appears still more promising. Fi-

nally, for the treatment of scarlet fever the Dicks, among others, have produced a serum which apparently has yielded favourable results in the acute stages of the disease. Scarlet fever, therefore, bids fair to follow diphtheria in making a welcome exit from a microbially harassed world.

Erysipelas

Erysipelas is an acute disease characterized by a special inflammation of the skin, accompanied by high fever. It is caused by a blood-dissolving (hæmolytic) streptococcus which Birkhaug has been able to differentiate from scarlet-fever and other streptococci. Erysipelas has frequently been a widespread disease, though with modern sanitation its incidence has been diminished. Since many cases of this disease follow wounds, abrasions, surgical operations, and childbirth, it is especially feared in hospitals. While there is little mortality associated with erysipelas, it is a very distressing infectious disease because of severe inflammation of all parts of the face, which inflammation may also extend to other parts of the body. There is, in fact, a close resemblance to poison-ivy swellings. The eyes are often so badly affected as to become closed. The fever runs high and delirium is a common symptom. Middle-aged men with alcoholic habits seem to contract erysipelas in great numbers. Their delirium is usually more severe than that which is observed in non-alcoholics. It is not uncommon in hospitals to send out a hurry-call for erysipelas patients who have escaped during a delirium.

Birkhaug has recently prepared an antitoxin for the treatment of erysipelas which appears successful. For the production of this serum a faithful donkey served him well. The antitoxin treatment of erysipelas compares favourably with the antitoxin treatment of diphtheria, according to reports from the Bellevue Hospital in New York City, where there are always a great number of cases of erysipelas. To judge from this report, erysipelas is conquered as far as any immediate danger of life is concerned; patients are able to leave the hospital sooner, and there are fewer complications than formerly. Since these conclusions come from a hospital whose experience is perhaps the most extensive in this country, one is encouraged to believe that the antitoxin treatment of erysipelas has robbed the disease of its terrors.

2. THE COMMON COLD, PNEUMONIA, MENINGITIS, AND GONORRHŒA

"You'll catch your death of cold," is the parental admonition against which youth universally rebels. The gallant young swain shrinks from the contemptuous glance he may expect from his best girl should he appear swinging a bedraggled umbrella, adorned in humid raincoat and a weighty pair of rubbers. Nor is the gay young charmer any less sensitive to the figure she cuts in similar paraphernalia. If only the safeguards against inclement weather were a little less cumbersome and a little more æsthetic, parents might stand a better chance of having their advice taken. So, for one reason or another, the common cold flourishes and pneumonia is not far behind.

The common cold, usually not serious in nature, passes so readily from individual to individual that it assumes considerable significance in daily life. "The condition is of great importance because of the great loss of economic efficiency which wholesale infection of a population with the common cold entails, and because of the fact that the catarrhal inflammation of the nose, throat and upper bronchi, which accompanies the cold, prepares a site for the lodgment and multiplication of influenza bacilli, pneumococci, streptococci, diphtheria bacilli, perhaps meningococci, and other organisms that may lead to more serious disease. Also, the sneezing, coughing and expectoration of individuals suffering from colds results in the promiscuous distribution of bacteria lodged, by chance, in the respiratory passages of such people. Carriers of virulent organisms of various kinds, such as diphtheria bacilli, meningococci, streptococci, pneumococcus types, I, II, and III, etc., begin, in the course of their colds, to distribute the virulent organisms they carry to others. They not only spread the virus that has given them the 'cold,' but scatter a spray which contains the virulent organisms to which they themselves are immune, and, therefore, not only directly infect susceptible contacts, but transmit to them directly a condition which will make it possible for these virulent organisms to lodge in their mucous membranes, and perhaps cause the secondary more serious diseases. A circuit of carrier distribution is so started, and it has been variously proved that during the

colder months of the year, when colds abound, the carrier rate of all respiratory diseases increases. . . . Prevention depends upon impressing these facts upon the public and laying stress upon the great danger of severe secondary disease. The avoidance of close contact, sleeping in the same beds, avoidance of the kissing of children, protecting companions from contamination by coughing and sneezing, disinfection of handkerchiefs, etc., may prevent the disease from going through families as is so often the case" (Zinsser).

We are all only too familiar with the cough and sneeze of the common cold, but we know little as to its cause. Whether it is due to a single microbe or to many is still debatable. Much research has failed to clarify the situation. Streptococci, pneumococci, and other infectious agents have been indicted as the specific cause of the common cold, but none of the evidence is particularly convincing. Nevertheless, from the standpoint of public health the importance of the common cold and the prevention of secondary respiratory diseases cannot be sufficiently stressed.

Pneumonia

As with the common cold, so with pneumonia. It is a disease characterized by fever and inflammation of the lungs, which may be caused by several microbes alone or in combination. The symptoms of pneumonia are familiar to most households. In a two-year-old baby for instance, according to Morse, there is a cold in the head for two or three days, without any real evidence of illness. Appetite is diminished. The baby becomes uncomfortable and feverish during the night, and towards morning vomits. He may even have a severe convulsion. Moving, coughing, and crying hurt him, while the temperature ranges over 104°F. A marked pallor and bluish lips are observed. Respiration is markedly increased as compared with pulse rate. The lower portion of the nose moves with respiration. Apart from a slight diminution in knee-jerks, nothing of special interest may be observed. Throat and heart may be normal. The diagnosis of pneumonia is made in spite of the absence of physical signs in the lungs. Pneumonia usually sets in abruptly with a very severe chill, lasting for about a half-hour. High fever is not far behind. Then come headache, an acute pain in the side, and a short, dry, but very painful

cough, accompanied by bloody expectoration. Following high fever and increased respiration for five to ten days, there comes a "crisis." The temperature suddenly drops very sharply. The other symptoms subside and the patient enters the convalescent period. Pleurisy, which is an inflammation of the surface of the lung, is an ever-present danger. There are many types of pneumonia, involving one or both lungs. The disease is always serious, for pneumonia is among the more fatal infections. Fortunately, it is readily diagnosed. Nursing, in a sense, is the most important feature of treatment, because pneumonia is essentially a self-limited disease, and little can be done to alter its course.

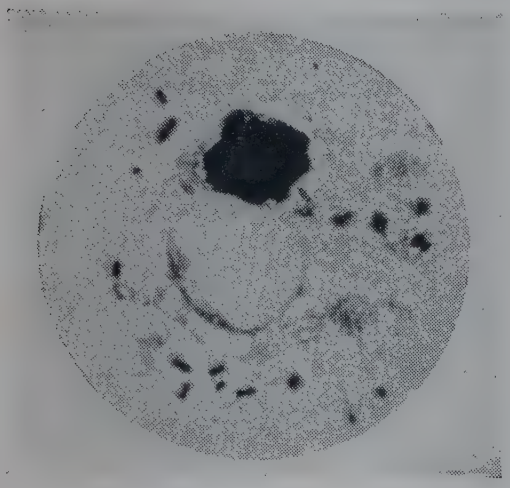


FIGURE 39

Encapsulated pneumococci, the cause of pneumonia, in pairs (blood cells in centre). (After Jordan.)

The most common microbe causing pneumonia is the pneumococcus, variously known as "*Diplococcus*," "*Streptococcus*," or "*Micrococcus pneumoniæ*," and "Fränkel's pneumococcus," named after its discoverer. (See fig. 39.) The first-named is the most descriptive term, since the form of the pneumococcus is probably its most reliable criterion of identification. The typical pneumococcus is a spherical or oval micro-organism, pointed at one end, or lancet-shaped, usually occurring in pairs. Hence the name "diplococcus." The pneumococcus may occur singly or in short chains resembling the streptococcus; or it may occur in tetrads or in clusters (dividing in two planes, which gives it the name "micrococcus"). A definite, fairly wide capsule surrounds each pneumococcus or pair of pneumococci. By special staining methods the capsule is easily demonstrated in fresh sputum or in exudates in the early stages of the disease. Pneumococci stain readily with most of the ordinary dyes and are Gram-positive.

Several years before the relation of the pneumococcus to pneumonia was established, Friedländer claimed that a short encapsulated bacillus known as the "*Bacillus mucosus capsulatus*," or "Friedländer group," was responsible for most pneumonias. Subsequent investigation showed him to be in error,

although the bacilli he described have disease-producing properties, particularly in the nose and throat.

Pneumococci do not lend themselves readily to cultivation in the laboratory because of fastidious requirements due to their parasitic existence. Ordinary bacteriologic media yield sparse, if any, growth. The addition of whole blood or serum, however, enhances growth, again indicating the parasitic nature of pneumococci. Other substances, such as glucose or glycerine, are of value, as are media especially adapted to their development.

During artificial cultivation pneumococci tend to die off rapidly, owing to the formation of acids which prove noxious — a perfect illustration of bacteria being their own worst enemies. In sputum they live longer, because of the protection afforded them against such adverse influences as drying. In fact, it has been shown that in dried pneumonic sputum the microbes may survive for as long as fifty-five days. When expelled into the air in a fine spray, as in coughing or sneezing, the pneumococci cannot survive for more than a few hours.

The temperature range for the artificial cultivation of pneumococci is exceedingly narrow — namely, from 77 to 107 degrees Fahrenheit. The best growth is obtained at about body temperature or 100°F. This, again, emphasizes the parasitism of pneumococci, for it shows how well adapted they are to the conditions obtaining in the human body.

Pneumococci may be isolated from sputum or other materials containing several kinds of microbes by streaking the surface of blood-agar plates with the infected material. Colony-formation is characteristic: small, round, transparent, flat, and moist. In this as well as in other respects pneumococci resemble the streptococci, to which they are closely related.[1] Another method, simpler than plating, for the isolation of pneumococci is to inject into white mice a small amount of the suspected sputum or other material. Mice will die in about twenty-four hours if virulent pneumococci are present and the organisms can be recovered from their hearts' blood. Pneumococci may be preserved for long periods of time by keeping the dry infected spleen of white mice in the ice-chest or by freezing broth cultures dried in a vacuum.

[1] Unlike streptococci, pneumococci dissolve bile salts and ferment the sugar inulin.

Why is the artificial cultivation of pneumococci of importance, one might inquire, for do they not cause enough trouble naturally? The answer to such a query takes us deeply into serologic questions dealing with agglutination and protection tests on animals. Without going into detail, it is on the basis of such tests that pneumococci may be more or less sharply differentiated into four main types, numbered accordingly I, II, III, and IV. Types I and II are the typical pneumococci, Type III represents what was formerly termed *Streptococcus mucosus*, and Type IV is a heterogeneous group which includes all of the true pneumococci that cannot be placed in the first three types. Zinsser says: "This fourth group is merely a matter of convenience of nomenclature, since few of these organisms are related to each other. They represent a sort of attic into which unclassifiable pneumococci have been thrown for the present, until they can be sorted out."

Laboratory identification of the type of pneumococcus responsible for any individual case of pneumonia is of importance since fairly successful efforts have been made to fight the disease with serums, vaccines, and antibody solutions. Obviously a serum for Type I pneumococcus would not avail against the pneumonia produced by a Type II infection. Similarly, mixed vaccines liberally advertised to contain all the organisms causing pneumonia are not acceptable to the conservative physician, who regards them as "shot-gun" preparations, since they bespatter rather than strike the target. There is, nevertheless, a growing body of evidence to indicate that the use of serum or refined antibody solution is of benefit to patients who are treated *early*.

Pneumonia is always with us, being at once one of the most widespread and fatal of infectious diseases of the temperate zones. It accounts for about one death in every ten. While cases of this disease occur throughout the year, they increase in incidence during the colder months.

Pneumonia may occur at any age, the incidence being higher in the very young and the very old. It occurs more frequently in males than in females and appears to be more fatal among Negroes than among white persons. Over ninety per cent of acute lobar pneumonia is caused by pneumococci. The other ten per cent may be caused by streptococci, or other micro-organisms. Pneumococci, incidentally, cause, not only pneumonia, but other

inflammatory diseases as well, as, for example, middle-ear and heart infections, meningitis, etc. Among alcoholics three-fourths of the cases of pneumonia die. Cabot says: "This is one of the best established examples of the harm that alcohol does in people whom it does not make drunk. A man who is never drunk at all but is chronically alcoholic, when he gets pneumonia is three times as apt to die as the total abstainer."

Lobar pneumonia, which affects the entire lung, must not be confused with broncho-pneumonia, which is an infection of the bronchi, or tubes which run into the lung. Broncho-pneumonia is a "patchy" type of pneumonia and runs a different course from true lobar pneumonia. There is no crisis. Often broncho-pneumonia is a complication of other diseases, such as measles, whooping-cough, or diphtheria. In children the nerve to the palate may become affected, giving to the speech a decidedly nasal twang and causing fluids, when drunk, to run through the nose. Broncho-pneumonia is greatly to be feared after all surgical operations. It is frequently contracted by old people, particularly those who suffer from heart-disease.

In times of peace, pneumonia is responsible for approximately ten per cent of all deaths, but in times of war it causes a considerably greater mortality, owing to the lowered resistance incident to unsanitary living conditions and exposure to wet and cold. A heightened virulence of the microbe also plays an important part in the ravages of this disease. From these considerations it is not difficult to understand how disastrous pneumonia is in institutional life, where overcrowding, together with lack of air and exercise, are conducive to the spread of infection. About one-fourth of all adult cases die. Consequently it is of vital interest to each individual (and to the community as well) that individual resistance be kept high and not permitted to be depressed by colds, exposure, fatigue, malnutrition, etc. In this way the danger of epidemics may be diminished and the incidence of individual cases reduced.

Meningitis

Meningitis, an infection of the meninges, or lining of the brain and spinal cord, like pneumonia may be caused by a number of different microbes. Meningitis may be a primary disease,

in which event it is caused chiefly by the meningococcus; or it may be a secondary disease following typhoid fever, influenza, pneumonia, or middle-ear diseases, especially in children. In the latter instances the infectious microbe is carried by the blood-stream from the site of inflammation to the meninges, generally causing death. Epidemics of meningitis are almost invariably due to the meningococcus, technically known as "*Diplococcus intracellularis meningitidis*," which is the specific cause of cerebrospinal fever, as differentiated from cerebrospinal meningitis, which may be caused by a variety of organisms.

The meningococcus was first identified by Weichselbaum in 1887. (See fig. 40.) Like the pneumococcus it occurs most often in pairs (diplococci), but may also occur in tetrads, and has therefore frequently been called *Micrococcus meningitidis*. In appearance meningococci bear a striking resemblance to gonococci (next to be described), being slightly flattened, biscuit-shaped cocci of variable size. Meningococci are easily stained by the ordinary dyes and are Gram-negative. Some strains of meningococci are easily cultivated artificially, while others are very fastidious, requiring blood or even special "hormone," egg-yolk or other enriched media. Like pneumococci these diplococci have a narrow temperature range, body heat, or about 100°F, being most favourable. They will not grow at ordinary room temperature. Meningococci require oxygen and are stimulated by carbon dioxide (about ten per cent). Ordinarily these micro-organisms die rapidly on artificial media, but the addition of precipitated chalk (one per cent calcium carbonate) neutralizes the acids formed which would otherwise kill them. They succumb readily upon exposure to sunlight or other disinfecting agents. Again, like pneumococci the meningococci are grouped into types on the basis of serologic tests. These furnish the basis for determining the kind of serum to be used for meningitis.

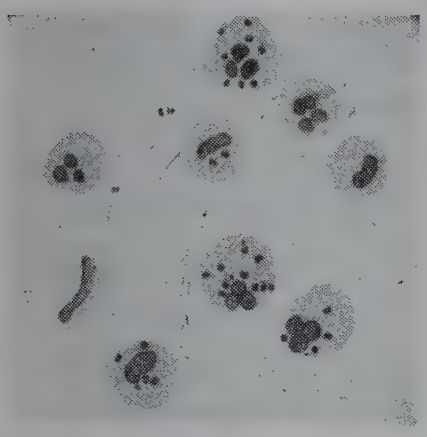


FIGURE 40

Meningococci, the cause of meningitis, mostly within pus cells. (After Jordan.)

Meningitis, as previously stated, is a disease which consists in the formation of pus in the meninges and generally affects the

base of the brain and the spinal cord, unlike other common bacterial infections. Meningitis like pneumonia is most prevalent in cold and inclement weather, and serious epidemics have not been infrequent. Many of the Napoleonic campaigns testify to this. In 1904–5 an epidemic of meningitis resulted in seven thousand cases in New York City alone. The disease is rapidly transmitted from individual to individual through secretions from the nose and throat. When resistance is low, infection occurs, but even healthy persons are "carriers"; that is, they may transmit the microbes to other individuals without coming down with the disease themselves. To quote Zinsser: "Infection of a healthy individual from a case is of very rare occurrence, and since there are in every epidemic a very much larger number of carriers than cases, the carrier is the chief epidemiological problem. . . . This rareness of transmission from cases to the healthy is in our opinion due to the peculiar conditions of susceptibility that prevail in relation to meningitis, and the fact that the number of people with whom the sick come in contact is relatively small. The susceptibility of man to meningitis is a curious one, different in some aspects from susceptibility relations to almost all other infections, except perhaps poliomyelitis [infantile paralysis]. In the general population there seems to be a great variability in individual susceptibility to infection with the meningococcus, a variation which can be traced to no determinable cause. Unlike pneumonia, temporary fluctuations in well-being, produced by respiratory disease, malnutrition, exposure to cold, etc., do not seem to play a determining rôle. The disease indiscriminately picks out individuals here and there, some of them in the most robust health, strong and hardy, while sparing associates who may be feeble and run down. It is obvious that some individuals are normally resistant and will not come down, in spite of considerable exposure, while others are delicately susceptible. The difference may possibly have been produced fortuitously by the fact that some individuals may have been carriers at one time or another, and have become, thereby, spontaneously immunized."

Several forms of cerebrospinal fever are recognized and classified as malignant, ordinary, and anomalous (Osler and McCrea). The first is most sudden, severe, and fatal. In its ordinary form the disease sets in suddenly with headache, severe chills, and

vomiting. Fever runs about 101°–102°F., and the number of white blood cells (leucocytes) increases. Painful stiffness of the neck is an early and important symptom. Headache increases, while light and sound become annoying to the patient. Squint (strabismus) is a characteristic symptom. Restlessness and irritability become marked, especially in children. Tremor and spasm of the muscles of arms, legs, and face are present and rigidity is common. Great sensitiveness along the spine is not infrequent. Pronounced psychic symptoms such as delirium and erotic outbursts are present at the onset. The delirium gives way in a few days to stupor, which in turn deepens into coma. A spotted rash, which originally gave the name of "spotted fever" to this disease, appears. It is variable in nature. The disease may run a course of from a few hours to several months. More than half of the deaths occur within the first five days. A sudden fall in temperature, which elevates the spirits of the family, is actually an ominous portent. Not only is the disease very severe in its acute stages, but convalescence is also very trying. Relapses and complications often occur.

It is to the bacteriologic laboratory that we must turn in the hope of controlling the spread of meningitis. Spinal fluid must be withdrawn as early as possible in patients who show any suspicious symptoms, so that a search for meningococci may be made, and if they are present, the type identified.

Serum treatment should follow immediately. The mortality without serum treatment has been between sixty and eighty per cent. By employing serum the mortality rate has been reduced to about thirty per cent, or less than half. Possibly the most important factor in the use of serum lies in its early administration. It has been shown by Flexner that in cases treated before the third day only 18.1 per cent died, while in cases treated from the fourth to the seventh day 27.2 per cent died. Contrast 18.1 per cent mortality after serum treatment with 80 per cent mortality before the introduction of serum therapy, and credit the tremendous difference to the science of bacteriology.

Closely resembling the meningococci in stained preparations under the microscope and early growth on solid mediums are the Gram-negative *Micrococci: catarrhalis, flavus, etc.*, which are also found in the mucous membranes of the respiratory tract. The

former may cause catarrhal inflammation, the latter are found in the normal throat. It is most reassuring to have a laboratory diagnosis naming these micrococci rather than meningococci — hence the value of prompt examination in suspected cases. Another Gram-negative micrococcus resembling the meningococcus and even more closely the gonococcus, presently to be described, is *Micrococcus melitensis*, which causes Malta fever in animals, a disease largely confined to the shores of the Mediterranean. More than one bacteriologist, however, has contracted Malta fever during the course of experimentation.

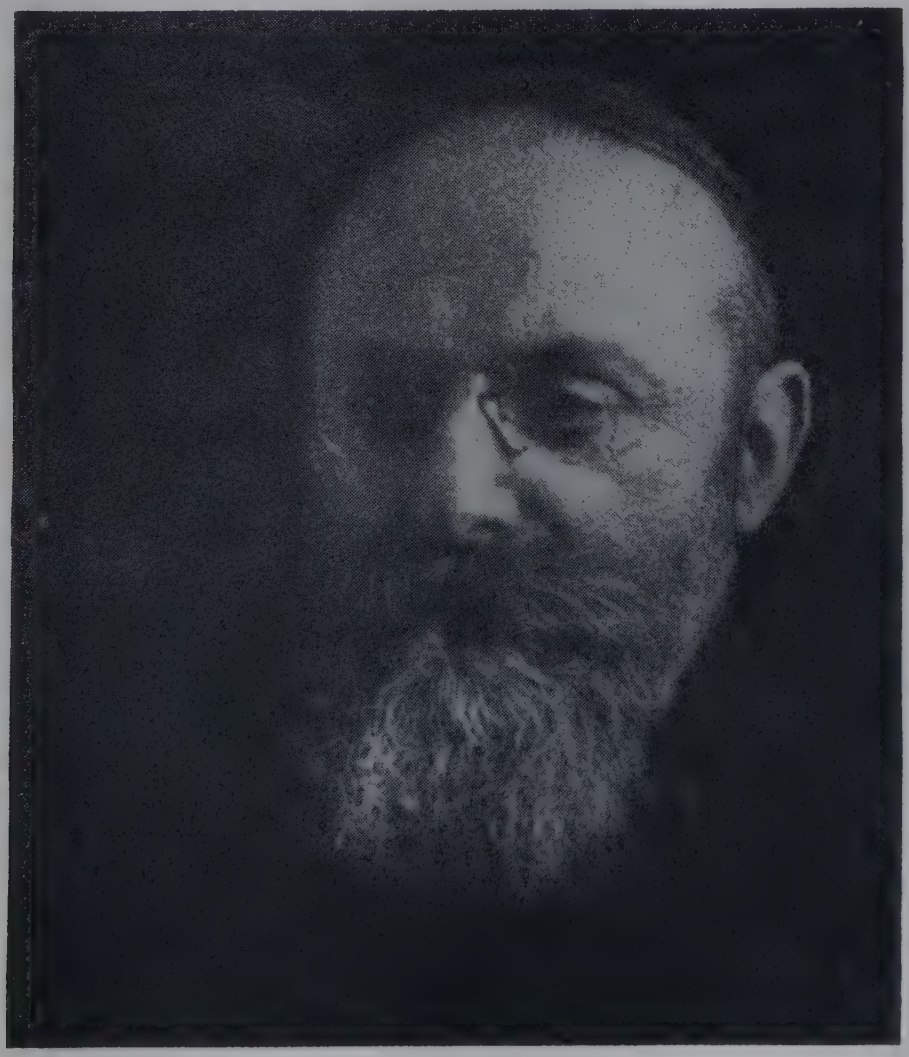


FIGURE 41

Neisser, discoverer of the cause of gonorrhœa. (After Deschiens.)

Gonorrhœa

Gonorrhœa, the most prevalent of venereal diseases, is caused by the gonococcus. This organism, like the pneumococcus and meningococcus, occurs chiefly in pairs, and therefore earns the

name of *Diplococcus gonorrhœæ*, or *Micrococcus gonorrhœæ*, because it also divides in two planes. To Neisser, the great German bacteriologist (see fig. 41), belongs the credit for the discovery of the gonococcus, in 1879, and to Bumm, in 1885, the distinction of cultivating it artificially and proving that it could produce the disease when reinjected into man.

In form, gonococci appear under the microscope as pairs of cocci flattened along the surfaces facing each other, which gives them a characteristic biscuit, coffee-bean, or kidney shape. (See fig. 42.) Like meningococci they stain with the ordinary dyes and are Gram-negative. Similarly they are difficult to cultivate artificially, requiring the addition of enriching substances, such as blood-serum, to ordinary nutrient media. They have a narrow temperature range, growing best at body heat and not growing above 101°F. or below 86°F. Gonococci do not represent a single type of diplococcus, but may be classified into sub-groups, depending on sugar fermentation and serologic tests. A further interesting differentiation has been brought out by Louise Pearce, who showed that species of gonococci isolated from adult males were distinct from those obtained in vulvovaginitis in female children.

FIGURE 42

Gonococci, the cause of gonorrhœa. (After Conn and Conn.)

Gonorrhœal infection is entirely a human affliction, for it occurs only in *homo sapiens*. The gonococcus produces acute and chronic disease not only in the genital organs of men, women, and children, but in the urinary system, the joints, and the mucous membranes of the eye as well. Sterility in women and blindness in new-born children are frequently the curse of the gonococcus, often ignorantly bestowed and innocently acquired. The practice of instilling a two-per-cent solution of silver nitrate in the eyes of every child at birth has now mitigated one of these evils.

It has been generally estimated that one out of every ten persons in the United States suffers from venereal disease at one time or another. Gonorrhœa is the most common infection in this category. Ignorance, indifference, and prudery are responsible for the undue prevalence of this disease, which in certain sociologic aspects has been regarded as equivalent to or even

more serious than syphilis. The prevention and treatment of gonorrhœal infections has made considerable progress in recent times. In fact, all too frequently it may lead to a false sense of security. Many a man contracts gonorrhœa in the days when he is sowing his wild oats, takes treatment for it, and marries under the impression that he has been cured, only to infect his unsuspecting wife. A bacteriologic examination should be universally required to ensure against possible transmission of the disease after it has been controlled, for the gonococcus may persist in the mucous membranes for long periods of time.

Gonorrhœa in adults is almost invariably transmitted by sexual contact. The gonococcus may, however, remain viable on towels, clothing, or bedding, for short periods of time and thus prove infective in rare instances. In female children vulvovaginitis, caused by the gonococcus, is not transmitted by sexual contact but by infection from toilet seats, etc. The disease spreads like wildfire through schools and orphan asylums. It does not yield readily to treatment, sometimes lasting for years. Usually it disappears by the age of puberty and fortunately it has none of the serious consequences in the genital tract that gonococcus infection has in adults. Children should be trained to cover public toilet seats with toilet-paper before sitting upon them. Every adult should also attempt to escape infection by following the same practice.

The prevention of infection after exposure was effectively accomplished in the United States Army during the World War by the injection of a small amount (two teaspoonfuls) of a two-per-cent protargol solution into the urethra. This prophylactic measure should be twice repeated. Its efficiency depends to a great extent upon its early use after intercourse, for delay seriously impairs the chances for successful treatment.

Chapter VII

DISEASE-PRODUCING BACILLI

I. DIPHTHERIA

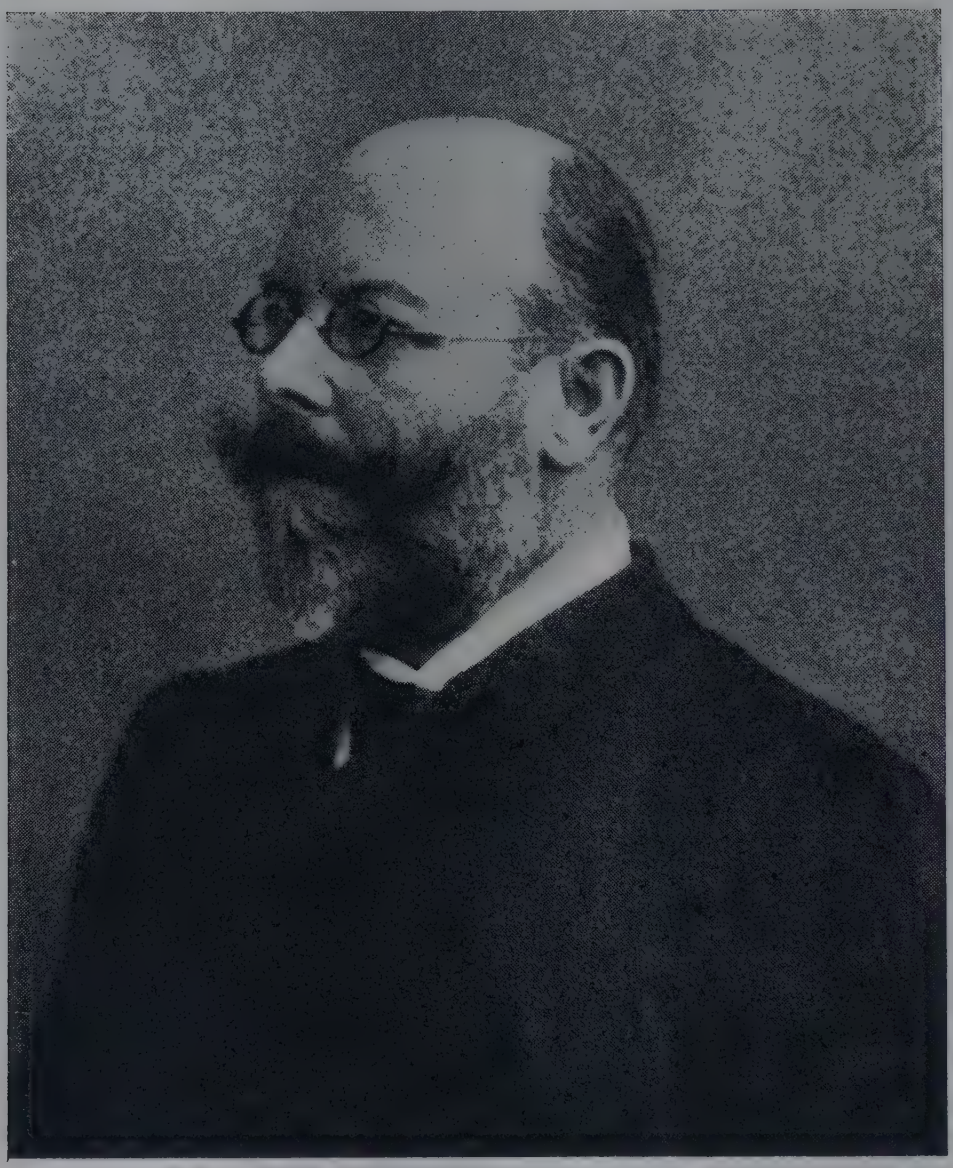


Figure 43

Löffler, discoverer of the cause of diphtheria.
(After Deschiens.)

Diphtheria, as a disease, was first accurately described over a century ago and given its name by Bretonneau (1821). But it was not until more than sixty years later (1883–4) that Klebs and Löffler (see fig. 43) isolated the causal organism, *Bacillus diphtheriæ* (long known as the Klebs-Löffler bacillus). The terrors of

diphtheria are due to a powerful poison or toxin which is produced by the bacillus at the site of intense inflammation in the throat. The diffusion of this soluble toxin throughout the body gives rise to symptoms so severe that they may result in death.[1]

No one minds having his pulse taken, but when the family doctor reaches for a teaspoon to depress the tongue, we all gag.

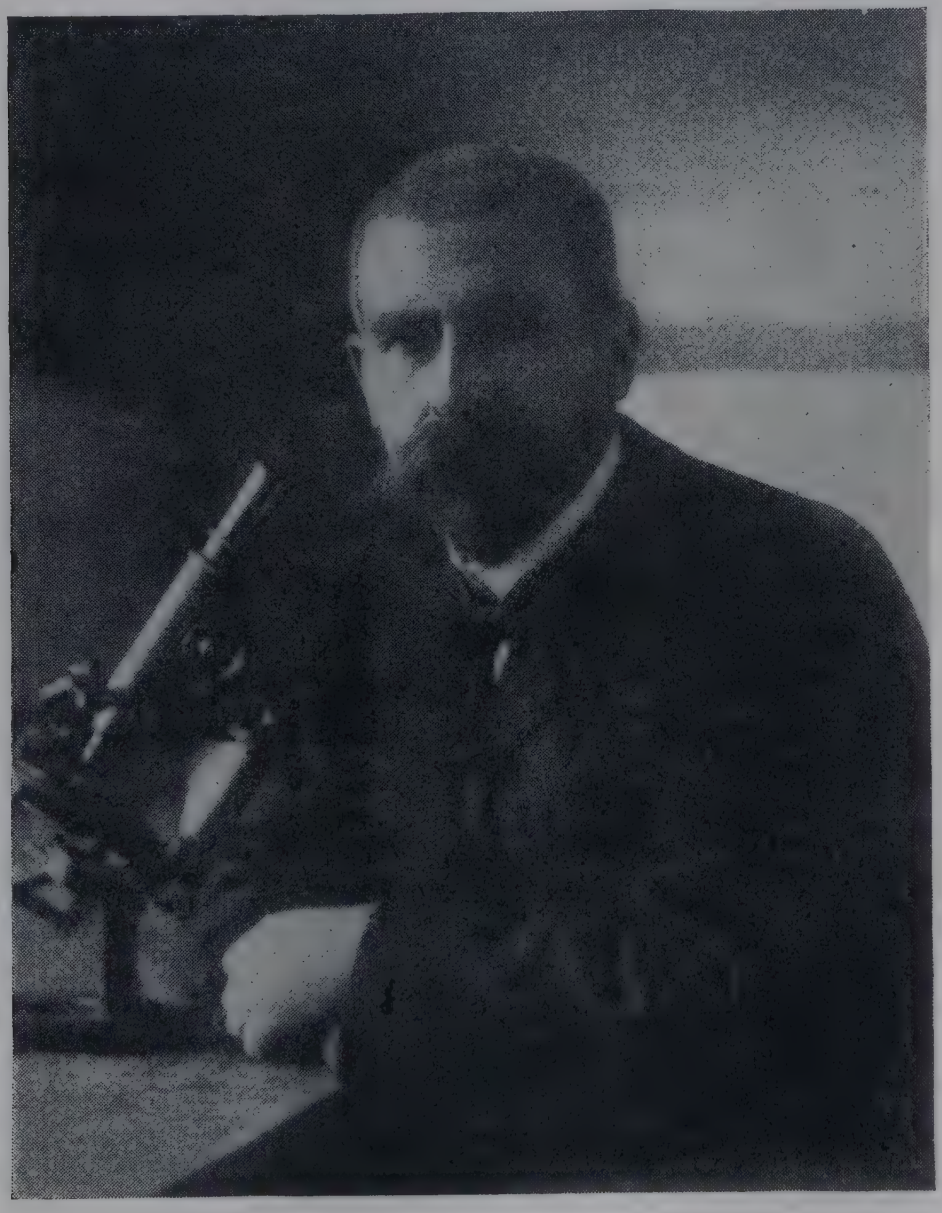


FIGURE 44

Roux, discoverer of diphtheria toxin. (*After Manuel.*)

At no time is this practice more necessary than when diphtheria is suspected, for the disease is characterized by inflammation of the mucous membranes of the throat and the formation of a

[1] That the diphtheria bacillus elaborates this potent toxin, which may be separated from the living microbe by filtration through unglazed porcelain, was demonstrated by Roux and Yersin in 1888–9. (See fig. 44.)

"pseudo-membrane" (that is, not a true cellular covering). Then, too, there are general symptoms of increased temperature, rapid pulse, headache, muscular pains, and eruptions which are caused by the toxin produced by the diphtheria bacillus. Diphtheria is often fatal. Death may be due to the toxin alone, to obstruction of the larynx, to broncho-pneumonia, or even to blood-poisoning by bacteria other than the diphtheria bacillus, such as streptococci, acting as secondary invaders.

A curious feature of diphtheria epidemics is that they occur in waves at five- and ten-year intervals. The disease claimed a mortality of about 150 per 100,000 in New York City according to statistics of a generation ago. Among its noted victims must be included George Washington. Like pneumonia and other respiratory diseases there is an increased number of cases of diphtheria in cold and inclement weather.

Diphtheria, strangely enough, is more common among country than among city folk; and the children from affluent homes seem more susceptible to the disease than children who live in the tenement districts. The explanation for these apparent paradoxes seems to lie in the fact that continual exposure to this bacillus, as must necessarily be the case under congested conditions, stimulates sufficient resistance to confer immunity. The hothouse child and the isolated farmer therefore suffer because of segregation from their fellows. Although diphtheria attacks adults, it is among children that it takes its greatest toll and it is therefore rightfully regarded as a "children's disease."

"The cause of epidemic outbursts is doubtless due to a fortuitous combination of such circumstances as a new crop of susceptible children, a particularly virulent strain of the bacillus, opportunity for contact, and environmental factors favoring the spread of the infection. Just as a spark in a forest may cause a brush fire or a conflagration, depending upon the amount of plant growth, its distribution, its condition as to dryness, the direction and force of the wind, the topography and nature of the soil, and any other conditions, so diphtheria and other infections will smolder or burst into flame, depending upon similar factors." [1]

[1] M. J. Rosenau: *Preventive Medicine and Hygiene.* New York, D. Appleton & Co., 1927.

Diphtheria is readily transmitted from individual to individual via the throat and nose discharges of diphtheria patients, convalescents, and healthy "carriers." It has been estimated that in New York City alone there are more than sixty thousand carriers. Diphtheria is only one of many diseases which are transmitted by secretions from the mouth and nose — so that the following quotation from Chapin may serve as a caution for pneumonia, influenza, whooping-cough, tuberculosis, and a number of other infectious diseases, as well as diphtheria. "Not only is the saliva made use of for a great variety of purposes, and numberless articles are for one reason or another placed in the mouth, but, for no reason whatsoever, and all unconsciously, the fingers are with great frequency raised to the lips or nose. Who can doubt that if the salivary glands secreted indigo the fingers would not continually be stained a deep blue, and who can doubt that if the nasal and oral secretions contain the germs of disease these germs will not be almost as constantly found upon the fingers? All successful commerce is reciprocal, and in this universal trade in human saliva the fingers not only bring foreign secretions to the mouth of their owner, but there, exchanging it for his own, distribute the latter to everything the hand touches. This happens not once, but scores and hundreds of times during the day's round of the individual. The cook spreads his saliva on the muffins and rolls, the waitress infects the glasses and spoons, the moistened fingers of the peddler arrange his fruit, the thumb of the milkman is in his measure, the reader moistens the pages of his book, the conductor his transfer tickets, the 'lady' the fingers of her glove. Everyone is busily engaged in the distribution of saliva, so that the end of each day finds this secretion freely distributed on the doors, window sills, furniture, and playthings in the home, the straps of trolley cars, the rails and counters and desks of shops and public buildings, indeed, upon everything that the hands of man touch. What avails it if the pathogens [disease-producing microbes] do die quickly? A fresh supply is furnished each day. Besides the moistening of the fingers with saliva and the use of the common drinking cup, the mouth is put to numberless improper uses which may result in the spread of infection. It is used to hold pins, string, pencils, paper and money. The lips are used to moisten the pencil, to point the end for the needle; to

wet postage stamps and envelopes. Children 'swap' apples, cake and lollypops while men exchange their pipes and women their hair pins. Sometimes the mother is seen 'cleansing' the face of her child with her saliva-moistened handkerchief, and perhaps the visitor is shortly after invited to kiss the little one. Children have no instinct of cleanliness, and their faces, hands, toys, clothing, and everything that they touch must of necessity be continually daubed with the secretions of the nose and mouth. It is well known that children between the ages of two and eight years are more susceptible to scarlet fever, diphtheria, measles and whooping-cough than at other ages, and it may be that one reason for this is the greater opportunity that is afforded by their habits at these ages for the transfer of the secretions. Infants do not, of course, mingle freely with one another, and older children do not come in close contact in their play and they also begin to have a little idea of cleanliness."[1]

FIGURE 45

Diphtheria bacilli. (After Conn and Conn.)

Because of its great variability the diphtheria bacillus is one of the most interesting of disease-producing bacteria. In form it is usually a thin, straight or slightly curved rod with a peculiar club-shaped thickening. (See fig. 45.) Variations in length, thickness, and symmetry are the rule rather than the exception, even in pure culture. Irregularity of staining, which is characteristic, is also of great aid in diagnosis. Diphtheria bacilli stain readily with ordinary dyes and are Gram-positive. Special stains (such as that of Neisser) in young cultures bring out polar bodies, oval in shape and situated most frequently at the ends of the rod. *Bacillus diphtheriæ* may be cultivated on enriched media, especially those to which blood-serum is added. Like the pus-forming microbes just described, diphtheria bacilli grow best at body heat; but, unlike the former, they have a wider temperature range (from 66° to 108°F.) and are more resistant to adverse environmental conditions such as drying, freezing, and exposure to sunlight.

Diphtheria bacilli vary in their capacity to elaborate toxin, and by cultivation in suitable broth the production of toxin by different strains may be studied. Virulence is established by in-

[1] Chapin, quoted in Rosenau, op. cit., p. 189.

jection into guinea-pigs. The most virulent strains of diphtheria produce the strongest toxin. Yet there is no correlation between virulence and the degree of local inflammation in the throat. Thus Park, Williams, and Krumwiede state that "the most toxic bacillus we have ever found was obtained from a mild case of diphtheria simulating tonsilitis."

There are a number of bacilli closely resembling the diphtheria bacillus. These may produce a clinical picture identical with diphtheria, thereby making it impossible for a physician to make an early accurate diagnosis without a bacteriologic examination. These bacilli do not produce toxin; the diphtheria bacillus does.[1] The sooner the offending micro-organism is identified, the sooner can the diphtheria antitoxin be administered. Delay often proves fatal. The detection of carriers can also be determined only by a bacteriologic examination of the throat bacilli. This is imperative in tracing the source of a diphtheria epidemic and attempting to control it, for if a carrier is overlooked, he may continue to infect healthy individuals after the diseased patients are segregated.

To make a bacteriologic diagnosis of diphtheria it is necessary to take a culture as soon as possible from a suspected throat. The culture is made by swabbing the throat with a bit of sterile cotton, and then streaking the cotton on a suitable medium, such as Löffler's blood-serum agar. It is essential that the Löffler tubes be fresh and not out of some old stock kept in the drug-store. Further, the tubes should be incubated immediately at 100°F. for twelve to eighteen hours. At the end of this time colonies have grown and from them may be made fixed film preparations stained with Löffler's alkaline methylene-blue. A polar-body stain such as Neisser's reveals the characteristic diphtheria bacilli if present. To take stained smears of exudate directly from the throat may yield the same information, but is not so reliable a

[1] *Bacillus hoffmanni*, sometimes called the "pseudo-diphtheria bacillus," occurs in normal throats, but in stained preparations under the microscope appears as a shorter and thicker rod, usually straighter and without the characteristic polar bodies of the diphtheria bacillus. *Bacillus xerosis* is another micro-organism closely resembling the diphtheria bacillus, which is found in normal and inflamed membranes of the eye. Finally, there is a large group of so-called "diphtheroid bacilli," frequently present in the nose and throat, whose disease-producing properties have yet to be established.

procedure as first growing the micro-organisms on a solid medium and then making a microscopic examination.

A positive diagnosis of diphtheria calls for the immediate administration of diphtheria antitoxin. Delay may result in death, for the diphtheria toxin is so potent as to damage the heart beyond repair. At times the earliest administration of antitoxin may be too late. In such an event the family unjustifiably blames the physician. Recently, in New York, a child of Italian parents succumbed to diphtheria in spite of the use of antitoxin, but the frantic father killed the physician, whom he held responsible for the child's death.

Fortunately for the human race, it is so constituted that the blood of most adults normally contains a small amount of diphtheria antitoxin capable of safeguarding the individuals against the toxin of the diphtheria bacilli. Age is an extremely important factor in diphtheria, for as has been stated, it is essentially a "children's disease." But within the first six months of life, infants are rarely susceptible to the disease, thanks to the immunity which their mothers have passed on to them. From the second to the tenth year is the period of greatest susceptibility. After the tenth year the disease occurs less frequently.

The incidence and death-rate of diphtheria have been so markedly reduced by the use of the Schick test and injections of antitoxin that it seems highly probable that the dread disease of diphtheria will within a short time be practically wiped out of existence. The Schick test consists in the injection of a minute amount of standardized diphtheria toxin under the skin of the forearm. If sufficient antitoxin is present in the blood to protect against diphtheria, the reaction is called negative. But if a red wheal is formed at the site of injection, then the reaction is called positive, the obvious conclusion being that the individual is susceptible to infection by the diphtheria bacillus.

The Health Department of New York City has carried out the Schick test extensively and has carefully standardized outfits for performing the Schick test which have proved safe and satisfactory. Commercial laboratories have also placed on the market outfits for this purpose, so that the Schick test is available to every physician. In carrying out this test it is of utmost importance to "run a control" of heated toxin which is not poisonous

on the other arm, so that any pseudo-reactions due to sensitivity to the chemical constituents of the toxin preparation may be detected and discounted in cases which might otherwise appear to be Schick-positive.

If, as during an epidemic, haste is required to establish immunity, diphtheria antitoxin is immediately administered to the individuals who are Schick-positive. The more popular prophylactic preventive measure against diphtheria is the injection of a neutralized mixture of diphtheria toxin and antitoxin. This method has been used with conspicuous success by Dr. Park and his associates of the New York Department of Health in schools and children's institutions of all kinds. Children who were Schick-positive soon became Schick-negative on retesting. In Schick tests on over a hundred thousand schoolchildren in New York City and its environs eighty-five to one hundred per cent of susceptible children became immune after the first series of injections of toxin-antitoxin. From their results Park and Zingher (who has since become a martyr to science through accidental asphyxiation in his laboratory) conclude that it is advisable to inject toxin-antitoxin into children after six months of age so as to afford them protection against diphtheria at a time when the disease is most dangerous. In this way a population of children immune from diphtheria can be developed. Then there will be no more fresh cases of the disease and even the carriers of diphtheria bacilli can be eliminated.

The increasing use of antitoxin has likewise served to reduce the number of very severe cases of diphtheria. The dramatic spectacle of a generation ago when the country doctor, roused out of bed in the middle of the night, grasped his tracheotomy kit and hurried to the bedside of a child choking to death, saving it only by cutting the throat and inserting a tube that the child might breathe, has now become practically obsolete. Diphtheria is no longer so severe. And when it is, the modern hospital resorts to vacuum suction to remove the membrane which chokes the patient, rather than to slitting the windpipe.

Diphtheria is one of the infectious diseases which have yielded most to bacteriologic research. The cause of the disease and its mode of transmission are known. A definite curative agent has been developed. Even more, we have specific methods for

determining the susceptibility of each individual and preventing the disease or checking its spread.

2. INFLUENZA

"Influenza," "flu," or "grippe" are terms that cover a multitude of bacteriologic sins and a variety of clinical conditions. Many epidemics — and medical history has enumerated few more widespread than that of 1917–18 — have been ascribed to influenza. As in previous epidemics, the most recent came in two or three waves. The general symptoms of malaise, depression, fever, and congestion in the nose and throat, which precede graver respiratory conditions, are familiar. Usually there is pain in the back and in the extremities. Pronounced weakness is characteristic. Such weakness is far beyond the apparent disturbance to the organism and outlasts for weeks, or even months, the acute stages of the disease. Many patients who have recovered from a short attack cannot understand why that "all-gone" feeling should persist. It is extremely doubtful whether all epidemics of influenza have been caused by the same micro-organism. After the epidemic of 1889, however, Pfeiffer succeeded (1892) in isolating *Bacillus influenzæ*, which he considered to be the causal agent.

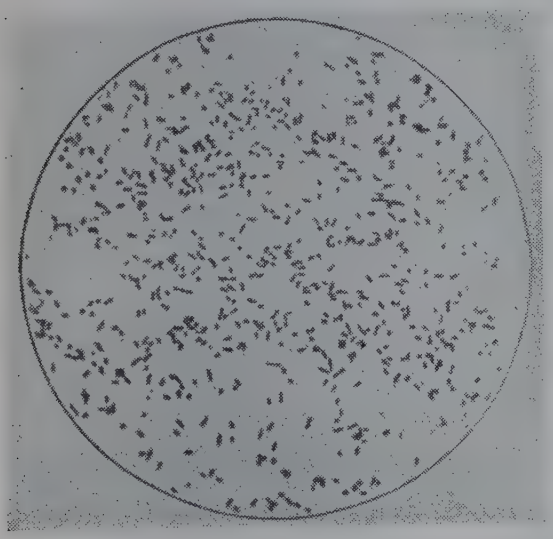


FIGURE 46

Influenza bacilli (magnified 1000 times.) (After Jordan.)

It is a very short, moderately thick rod which does not stain very readily with most dyes and unlike the diphtheria bacillus is Gram-negative. (See fig. 46.) Like a true parasite it grows best at body temperature and will usually not grow below 71°F. The solid colouring-matter of red blood cells, hæmoglobin, is almost essential for the adequate artificial cultivation of the influenza bacillus. Carbon dioxide (10 per cent), the gas we exhale, aids growth. In general, the influenza bacillus easily succumbs under adverse conditions such as drying and heat or when exposed to mild antiseptics.

A bacteriologic diagnosis of influenza is made after a study of cultures from the nasopharynx and sputum. Influenza bacilli may remain latent in the lung tissues for some time after an acute attack and then flare up again. To quote Park, Williams, and Krumwiede: "Consumptives frequently carry influenza bacilli for years and are particularly susceptible to attacks of influenza. Williams in the examination of sputa in cases of pulmonary tuberculosis, found abundant influenza bacilli in a large proportion of the samples of sputum from consumptives, and this not only in the winter but also in the summer, when no influenza was known to be present in New York. Taken together with results elsewhere, this indicates that at all times of the year many consumptives carry influenza bacilli about with them. Persons suffering from bronchitis and all other diseases affecting the mucous membranes, especially of the upper respiratory tract may harbor very many of these hemoglobinophilic bacilli. They may be found quite frequently also in apparently healthy persons."

But despite the wide distribution of the influenza bacillus and the fact that it is always isolated during an epidemic, it is far from established that it has caused all the epidemics ascribed to it. Thus in the severe epidemic of 1917–8 bacteriologic opinion was divided into three major groups, which held that the causal factor was: (1) A special streptococcus, of the *viridans* type (see page 73); (2) the influenza bacillus; (3) a filtrable virus — that is, an organism so small as to pass through a bacteriologic filter (see chapter XVIII). Without entering into the details of these different contentions, it now appears that the adherents of the filtrable virus theory, led by Olitzky, of the Rockefeller Institute for Medical Research, have established the most persuasive claim.

There are many influenza-like bacilli, just as there are many bacilli resembling the diphtheria bacillus — some slightly larger, some slightly longer and more slender. They have been isolated in certain epidemics of eye inflammation. Thus the Koch-Weeks bacillus is found in acute conjunctivitis (inflammation of the membranes of the eye); the Morax-Axenfeld bacillus in infections in the angle of the eye (angular conjunctivitis); zur Nedden's bacillus in ulcers of the cornea (outer layer of the eyeball). Closely allied is the bacillus of Ducrey, which causes soft

chancre, chancroid, or buboes, an acute inflammation in and about the genitals.

3. WHOOPING-COUGH

Whooping-cough is caused by a bacillus which is very similar to that of influenza. Both diseases, moreover, are easily transmitted from individual to individual, and epidemics are not infrequent. Whooping-cough is essentially a children's disease. Adults contract it but rarely. It works havoc in schools or infant asylums, spreading like wildfire. Most children are susceptible to the disease and, once directly exposed to it, have little chance of escape. Susceptibility to this disease is so general that Rosenau claims it causes at least ten thousand deaths a year in the United States alone — about as many as scarlet fever, if not more. Ninety-six per cent of deaths from whooping-cough are among children under ten years of age. Fatalities are often due not so much to whooping-cough itself as to the lung infections which follow. Tuberculosis and prolonged illness are not uncommon complications.

There are two important stages in whooping-cough, characterized by Osler as the "catarrhal" and the "paroxysmal" respectively. The catarrhal stage can scarcely be distinguished from an ordinary cold — a little fever, running nose and eyes, and a chest cough which is persistent. The typical "whoop" initiates the paroxysmal stage, which is unmistakable even at a distance. Coughing fits of varying duration and intensity are alarming to the child and anguish to its parents because the child gets blue and appears to be suffocating. The slightest internal or external stimulus is sufficient to bring on an attack: crying, swallowing, dust, etc. The disease lasts for about a month.

The whooping-cough patient is very infectious throughout the course of the disease and for a considerable period thereafter. Therefore strict isolation is required to prevent rapid spread of the disease. It has even been suggested that domestic animals, especially dogs, may transmit the disease. Quarantine not only is imperative in the acute stages of the disease, but should also be enforced until the cough is entirely absent. In this connexion, it is of interest to recount the experiences of the surgeon of a

recent MacMillan expedition to the Polar regions. He was struck by the fact that whooping-cough epidemics occurred among adult Eskimos as well as among children. Since the Eskimo is particularly susceptible to broncho-pneumonia, a quarantine was established in the Eskimo villages which prevented visitors from entering and transmitting fatal germs to them.

The cause of whooping-cough is a short oval-shaped rod, called "*Bacillus pertussis*" by its Belgian discoverers, Bordet and Gengou (1906). (See fig. 47.) It stains poorly with most dyes and is Gram-negative, like the influenza bacillus. But, compared with the latter, the bacillus of whooping-cough is slightly larger and more regularly oval in appearance. Bordet and Gengou had to devise a special glycerine-potato-blood agar on which to grow *Bacillus pertussis*, for it is very difficult to cultivate artificially. It grows best at body temperature, but also at lower temperatures.

FIGURE 47

Whooping-cough bacilli in a mass, above cells lining the throat. (After Jordan.)

If the sputum of patients in the early stages of whooping-cough be properly examined, *Bacillus pertussis* may be isolated, thereby establishing a positive diagnosis. It is rather difficult to distinguish between the bacillus of whooping-cough and that of influenza. Certain serologic tests are of value, however, in conjunction with artificial cultivation and microscopic examination.

The bacilli causing diphtheria, influenza, and whooping-cough have been here grouped for purposes of convenience. To be sure, they have certain important features in common; they are non-motile rods which do not form spores; and are primarily aerobic. But for man such considerations are academic compared with the fact that these bacilli cause acute respiratory infections which take a tremendous toll of human life. The tubercle bacillus also shares these properties, but because of its unusual social and economic importance it merits special consideration. This is reserved for the succeeding chapter.

Chapter VIII

TUBERCULOSIS

The Great White Plague is the bane of man's existence. John Bunyan designated it: "Captain of the Men of Death." Tuberculosis claims at least one-eighth of all deaths the world over. In the United States this figure is somewhat less, or approximately one-eleventh, according to the statistics for 1920. One of the most unfortunate features of tuberculosis is that the mortality is heavy during the most productive years of life. Fully one-third of all cases of pulmonary tuberculosis occur between the ages of fifteen and sixty. Death is not the only hardship of disease. Ill health entails financial burdens as well. The economic loss involved in tuberculosis alone has been calculated to be from a hundred and fifty to two hundred millions of dollars annually in the United States.

However ghastly the picture, there is at least one redeeming feature — namely, that the death-rate of tuberculosis has been declining steadily for the past fifty years. In London, for example, there has been a reduction of thirty-three per cent between 1901 and 1910. Osler and McCrae [1] call this "the most encouraging feature of modern sanitation," and attribute it to such factors as the improved social conditions (better housing, food, habits, etc.); education in hygiene; segregation of the sick; as well as prompt recognition and treatment of the disease. The two important elements are "fewer seeds, more stony soil." This brings to mind Knopf's admonition that to combat tuberculosis successfully requires the combined action of a wise government, well-trained physicians, and intelligent people.

The history of tuberculosis is familiar reading. For over two thousand years it has been considered a communicable disease, but it is surprising how little physical diagnosis has progressed beyond the master auscultation of Laennec (1781–1826). Simi-

[1] W. Osler and T. McCrae: *The Principles and Practice of Medicine.* D. Appleton & Co., 1925.

larly, scant progress has been made bacteriologically since Koch first discovered its cause, *Bacillus tuberculosis*, in 1882.

There is a recognizable disposition or constitution, inherited or acquired, which proves especially susceptible to attack by this organism. Environment, too, has an influence on bodily resistance. Thus, Trudeau, himself tuberculous, in consecrating his life to combating the disease, carried out an experiment which proves how important is a healthy environment. He showed that rabbits inoculated with tuberculosis if confined in a dark, damp place without sunlight and fresh air, rapidly succumbed, while others treated in the same way, but allowed to run wild, either recovered or showed very slight evidence of the disease.

Probably every person at some time or other before the age of puberty harbours the tubercle bacillus. Yet this does not mean that it must inevitably lead to tuberculosis. The "toxipathic factors," as Ritter calls them, come to the fore: bad housing conditions; mental disturbances (grief, worry, and fatigue); physical excesses (alcohol, tobacco, and venereal disease); mechanical causes (occupational diseases involving inhalation of dust or poisonous gases); infectious diseases (pneumonia, measles, and scarlet fever); accidents (automobile); shock (operations); conjugal influences (pregnancy or miscarriages); and, finally, actual contact with infected patients, the last of comparatively infrequent incidence.

No age is exempt, although, as Hippocrates pointed out, tuberculosis is more commonly fatal between the eighteenth and the thirty-fifth years. It might be added that the disease is highly infectious and perhaps contagious for children. It is believed, however, that there is scarcely any danger in an adult's associating with a tuberculous individual, as witness the absence of infection in doctors and nurses attending the patients. Likewise the possibility of contracting the disease in the marriage relation has been calculated (by Ritter) to be only about two per cent. On the other hand, there have been instances recorded which are more disturbing than these statistics. Thus Zasetsky recounts the case of a woman infected with tuberculosis who married three healthy men during a period of eleven years. The first husband died of tuberculosis seven years after marriage, the second died three years after marriage, and the third at the time of the report had

contracted the disease, the wife having in the mean while died of tuberculosis. Again, in a series of six thousand cases of tuberculosis Minnig has recently noted that when one of the consorts died, the mate was infected in fifty per cent of the cases, indicating that adult infection actually occurs. Where tuberculosis existed in one of the marital partners, he observes that "in the greater number of cases the man was more faithful to his wife than the wife was faithful to the husband." In an interesting experiment Dr. Lawrason Brown of Saranac Lake has shown that kissing carried more bacteria with it in the morning than in the evening — a finding which might stimulate not a little flippancy.

Tuberculosis attacks different races differently. Thus, one-third of all the deaths among the North American Indians in 1915 were due to tuberculosis. Negroes are notoriously susceptible, especially when they migrate to the cities, as they are doing yearly in greater numbers. "The Irish both at home and abroad are more prone to the disease than any other European races. The Jews have everywhere a low mortality from tuberculosis" (Osler). Because there is so much evidence of familial susceptibility to tuberculosis, it is sometimes mistakenly called a heritable disease. But it should be remembered that *there are no hereditary microbial diseases*. The offspring inherit only a predisposition to a disease.

The diagnosis of tuberculosis is beset with difficulties. Dr. James Alexander Miller, president of the National and New York Tuberculosis Associations, has said: "The clinical picture of pulmonary tuberculosis is not easy to trace in sharp outlines. This is due to an infinite variety of individual symptoms and signs. The onset of tuberculosis may be characterized by cough, malaise, loss of flesh and strength, blood-spitting, pleurisy with effusion, tuberculosis of other organs, hoarseness, indigestion and neurasthenia, any of which conditions may occur either singly or in combination."

Immediate examination should follow any suspicions engendered by the above-mentioned conditions. This includes a general physical examination, special examination of the chest, X-ray examination, and laboratory tests. Failure to recognize this disease in its early stages is likely to prove disastrous. Timely diagnosis and proper treatment offer much hope of recovery. As an illustration, we may cite a case described by Morse: "Eliza-

beth D. was twelve years old. Her father died of pulmonary tuberculosis before she was born. Her mother continued to live in the same house. Her only brother died of diabetes mellitus when he was ten years old. She had always been tall and slight and rather easily tired. She had had a dry cough for three months, which was more troublesome during the day than at night. She had had no pain in her chest and had raised almost nothing. Her mother thought that she had been a little feverish in the late afternoon and early evening. Her appetite was good and she had no disturbance of digestion. She had not been weighed for some months, but her mother thought that she had lost a little weight." Upon examination there was found diminished sound and movement, dullness, and râles in the right lung. The girl was tuberculous and immediate care and treatment was a necessity.

Tuberculosis may attack any organ of the body as disastrously as it affects the lungs. Thus we encounter tuberculosis of the face (which is very disfiguring), larynx, intestinal tract, kidneys, etc. "Galloping consumption," so called because of the rapidity of its course, is miliary tuberculosis, in which all the organs are attacked at once. Practically all hunch-backed children owe their deformity to Pott's disease, which is tuberculosis of the spinal column. Tuberculosis even attacks the brain. There was a time when it was believed that all brain tumours were due to tuberculosis. Now we know that only a small percentage of brain tumours can be ascribed to this cause.

Thanks to the efforts of the National Tuberculosis Association, the elementary facts of tuberculosis have been brought home to everyone through exhibits, newspaper publicity, motion pictures, and the printed word. Their efforts also comprise medical service, clinics, nursing, industrial work, open-air schools, and preventoriums. In addition to these, a definite program has been launched which includes rural, urban, and national problems. The public recognizes such benefits and has lent its financial support by donations, membership, and particularly purchase of Christmas seals. Tuberculosis can no longer be considered a merely personal matter, but, like many other infectious diseases, is a problem of vital importance to the community. This has culminated in community organization in the campaign against tuberculosis.

The bacillus of tuberculosis is a slender rod, often variable in form. (See fig. 48.) It is stained with difficulty and frequently presents an irregularly stained or granular appearance. The chemical composition of this micro-organism is of great significance in explaining why it is so resistant to adverse influences. Briefly stated, it contains eighty-six per cent of water and fourteen per cent of dry substances, one-fourth of which consists of fatty and waxy substances, insoluble in water, but soluble in alcohol and ether. The residue is chiefly nitrogenous (nucleoproteins, etc.). Cellulose (wood-fibre) is also found.

Because of its waxy content it is obvious that ordinary dyes penetrate the tubercle bacillus with great difficulty. Unlike most

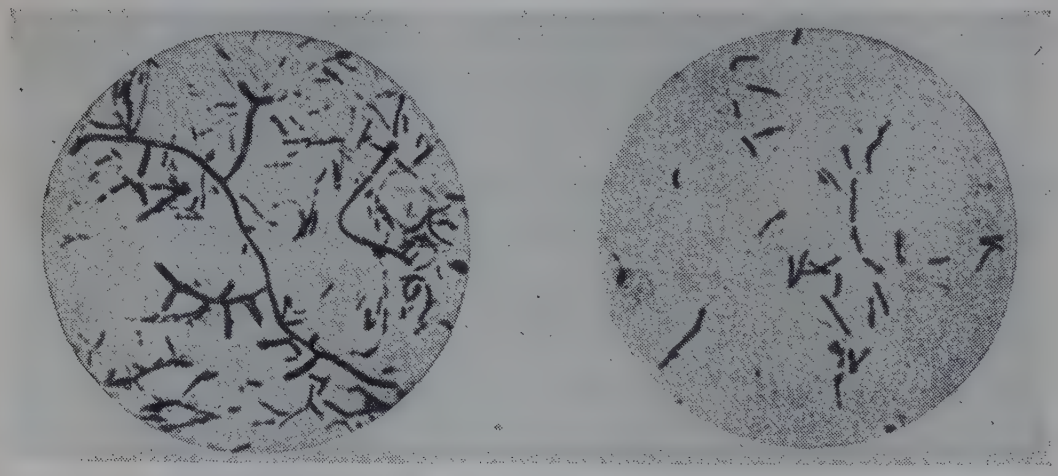


FIGURE 48

Tubercle bacilli. On the left, from culture; on the right, from sputum. (*After Marshall.*)

bacteria when once stained it is extremely difficult to decolorize the organisms even with strong acids. Consequently, this bacillus together with others of a kindred nature is called "acid-fast." A special staining procedure therefore must be employed which differentiates the acid-fast bacilli from others. Tubercle bacilli are frequently found in such small numbers that it becomes necessary to concentrate them. This may be done by dissolving out the mucus and cells present with peroxide of hydrogen or antiformin (a chlorinated lime-sodium carbonate solution used for cleaning brewery vats). Such drastic procedure kills other bacteria, but the resistant *Bacillus tuberculosis* emerges unscathed.

The tubercle bacillus is cultivated on artificial media with difficulty, for it grows very slowly under such conditions. The

addition of glycerine aids growth on nutrient agar (made with beef or veal broth) and on potato. (See fig. 49.) Because of the slowness with which the tubercle bacillus grows on artificial media and the danger of its being overgrown by contaminators, it is not practicable to utilize the common plating-methods already described, in isolating this micro-organism from tuberculous materials such as sputum or infected tissues. Here animals are invaluable. The method, for choice, is to inject the infected material into a laboratory animal, usually the guinea-pig. Since the infected material is likely to contain microbes other than the tubercle bacillus, an acute infection may occur immediately as a result of these other microbes. Usually the guinea-pig withstands this acute infection. But it gradually succumbs to the tubercle bacilli, so that in about a month it dies of tuberculosis. Then the tuberculous nodules are excised, minced, and plated on appropriate media. Such a procedure in the hands of experienced investigators yields colonies of *Bacillus tuberculosis*, usually free from foreign micro-organisms.

FIGURE 49

Tubercle bacilli growing on a glycerine agar slant. (After Marshall.)

From a biological standpoint, the tubercle bacillus requires a supply of free oxygen. It grows best at body temperature, but has a narrow range, since it will not grow below 86°F. Because of its waxy content the tubercle bacillus is extremely resistant to adverse influences. Dry heat 212°F. for one hour, or cold, which would kill most parasites, is well tolerated by *Bacillus tuberculosis*. In sputum, where mucus protects the microbes, the tubercle bacilli may remain alive for six weeks, and when sputum is dried, they may persist longer. Even in sewage they remain alive for weeks. Yet despite the great resistance of tubercle bacilli to dry heat and other adversities it is interesting to note that direct sunlight kills them readily.

The tubercle bacillus infects not only man, but a large number of animals as well, notably the cow, monkey, pig, and cat. Practically every organ and tissue of the body is subject to

invasion by this bacillus. The lesions are typical. In man small nodules are formed, and a cheesy degeneration of tissue takes place. The portal of entry of the tubercle bacillus is now generally believed to be the digestive tract — that is, the bacilli are swallowed. There is, however, a considerable divergence of opinion on this point. Droplet infection, resulting from sneezing or coughing, infection from sputum, as previously described, or from dust, are often regarded as being responsible for infection of the respiratory tract. Milk and butter from tuberculous cattle may cause infection by way of the digestive tract.

As a matter of fact, there are three distinct types of *Bacillus tuberculosis* — namely, the human, the bovine (attacking cattle),

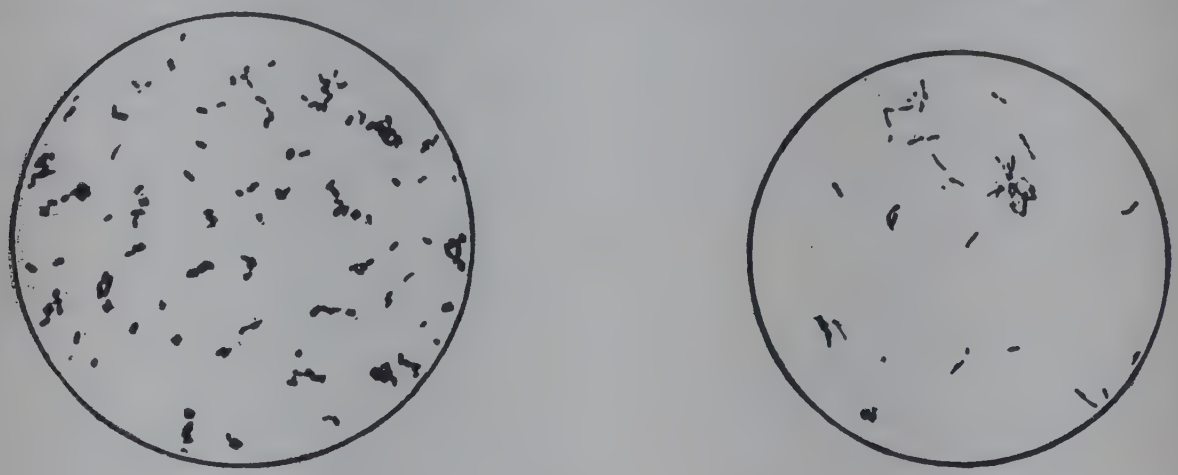


FIGURE 50

Tubercle bacilli. On the left, bovine; on the right, human. (After Park, Williams, and Krumwiede.)

and the avian (attacking birds). They differ slightly as to form and cultural characters. (See fig. 50.) There is considerable disagreement as to the danger to man from infection with bovine tuberculosis. There are those who contend that human beings become tuberculous by ingestion of milk containing the bacillus of bovine tuberculosis. On the other hand, Koch, the discoverer of the bacillus of human tuberculosis, maintained that the susceptibility of man to bovine tuberculosis is slight and that infection with milk, butter, or flesh of tuberculous animals is a very rare occurrence.

The consensus of opinion is that human adults are relatively immune from infection with the bovine type of tuberculosis. Susceptibility to bovine infection is relatively greater below sixteen years of age. Bovine tuberculosis appears to be responsible

for about one-third of all cases between the ages of five and sixteen years. Below five years the danger is greatest. The following figures, taken from Park, Williams, and Krumwiede, should offer sufficient evidence to demonstrate the necessity for strictest sanitary control of milk-supplies. They represent the actual number of cases encountered by these investigators in an unselected series of fifteen hundred tuberculous individuals.

Children under 5 years		*Children 5–16 years*		*Adults 16 years and over*	
Human Tuberculosis	*Bovine Tuberculosis*	*Human Tuberculosis*	*Bovine Tuberculosis*	*Human Tuberculosis*	*Bovine Tuberculosis*
292	76	131	46	940	15

In order to determine whether tuberculosis is present or absent in cattle (since the symptoms are not easily diagnosed in the early stages) the *tuberculin* test is applied. Tuberculin ("T. O.") was first devised by Koch and consists of a concentrated filtrate prepared from a glycerine broth culture of *Bacillus tuberculosis*. It is supposed to contain toxin. When a small amount of tuberculin is injected into a healthy animal (just as in the performance of the Schick test for diphtheria), there is no noteworthy effect. But when a tuberculous animal is so injected, there is a marked congestion in the tuberculous area, accompanied by sloughing of the tissue, fever, etc. A negative reaction is satisfactory, but a positive reaction condemns the animal. It is unfit to be a source of human food.

Tuberculin and antibody preparations of various kinds have also been utilized with some success to test human beings. Considerable caution, however, must be used in interpreting the results. Thus, Park, Williams, and Krumwiede state: "A positive reaction indicates the presence of a tuberculous focus but not necessarily of tuberculous disease. It tells nothing of the location, extent or activity of the lesion."

The hope of a specific treatment for tuberculosis, such as that of antitoxin for diphtheria, goes back to the days when Koch attempted to use tuberculin for curing tuberculous patients.

Many attempts have been made since to inject tubercle bacilli whose virulence has been reduced by different methods, in an effort to assist the human body to fight the inroads of the tubercle bacilli, but these have in the main proved unsuccessful.

The most hopeful attempt of recent times has been made by Calmette, of the Pasteur Institute (see fig. 51), with his "B C G"

FIGURE 51

Calmette, authority on the bacteriology of tuberculosis.
(After Deschiens.)

vaccine, prepared from attenuated tubercle bacilli. He has vaccinated a number of children giving every likelihood of contracting tuberculosis and prevented its onset. While final judgment must be suspended until more extensive results are obtained, there is reason to believe that Calmette's long experience and devotion to this problem will be crowned with success.

Dreyer's "defatted" vaccine has of late received much unde-

sired publicity. Theoretically promising, it has failed to prove of practical value. Sanocrysin, a gold salt prepared by Møllgaard in Copenhagen, upon injection into tuberculous patients is supposed to inhibit the bacilli. Investigators differ as to the efficacy of this chemical treatment of tuberculosis and are inclined to be critical, but further observations are required before a decision can be reached.

Specially prepared serums are of little value. One recalls the hocus-pocus of Friedmann's "turtle-serum." Spahlinger is now gaining notoriety in Switzerland for a secret treatment with pretentious claims and no substantial evidence. Scarcely a week passes without some sensational newspaper report of a new cure.

It would be a difficult task and a most unsatisfactory one to attempt to catalog the various "cures" for tuberculosis to which the public has so frequently turned. They vary from honest but misguided attempts to the sheerest quackery and their *raison d'être* is not hard to find. In desperation, the victim of the disease or those closest to him reach out for anything which offers a hope. Exploitation follows and disillusionment cannot be far behind. Nor can it be repeated too often that the choice of treatment in any disease should be placed in the hands of a reputable physician. It is unfortunate that he cannot always offer assurance of a speedy recovery, but he can at least guard against further dangers or expense which may result from the uncritical use of patent remedies. When the day comes that heralds a real cure for tuberculosis, the medical profession will be the first to acclaim it, as in the recent notable discovery by Banting of the use of insulin in the treatment of diabetes.

Chapter IX

LEPROSY

The bacillus of leprosy belongs to the same group of acid-fast bacilli which claims the tubercle bacillus, and therefore the resemblance between these two microbes is very close. Both cause diseases known to antiquity. There is evidence that leprosy prevailed in Egypt, India, and China some three or four thou-

Figure 52

Culion leper colony. (*After U. S. Public Health Reports.*)

sand years before Christ. Greek and Roman physicians, too, have recorded its occurrence. Old Peruvian pottery attests to its presence before Columbus visited these shores. But leprosy is not of frequent occurrence in the United States. There are only three centres in the United States where there are a sufficient number of lepers to constitute a problem — namely, Louisiana, Califor-

nia, and Minnesota. While it is difficult to ascertain the total number of lepers in these localities at the present time, it probably approximates five hundred. Today leprosy is most common in India (where there are more than a hundred thousand lepers), in China, in the Pacific islands, and in South Africa. The disease occurs in Norway, Russia, Canada, and Iceland as well. The colony established by the United States for the segregation of lepers on Culion Island in the Philippines numbers about five thousand. (See fig. 52.)

At one time it was thought that the disease was associated in some way with the constant eating of dried fish. But Hansen, in 1879, demonstrated that leprosy was caused by a specific bacillus, *Bacillus lepræ*. It bears a close resemblance to *Bacillus tuberculosis;* for it is a slender, acid-fast rod, possibly slightly less slender and less apt to present the characteristic granular appearance of the latter.[1] (See fig. 53.)

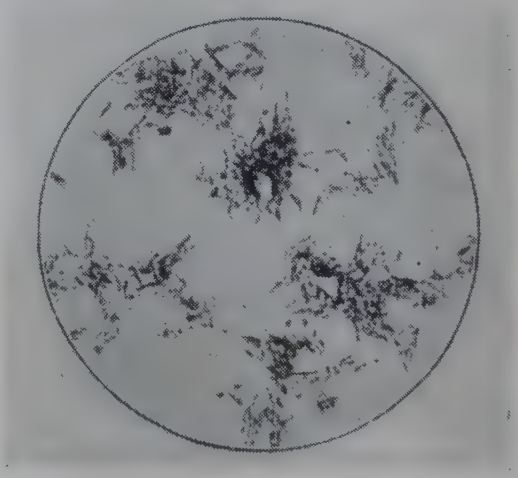


FIGURE 53

Leprosy bacilli. (*After Jordan.*)

The artificial cultivation of the bacillus of leprosy offers even more difficulty than that of the tubercle bacillus. Clegg was the first to grow it in the presence of amœbæ. Duval not only corroborated this observation, but went further in developing a specially digested protein medium for its growth. Apparently, he also succeeded in infecting animals with leprosy bacilli — a very difficult matter.

Leprosy, it is generally believed, is transmitted by secretions

[1] Closely approximating the bacilli of leprosy and tuberculosis is the smegma bacillus. It is more variable in size and appearance, and, although more easily stained than the tubercle bacillus, it nevertheless belongs definitely with the acid-fast bacilli. Because of the fact that it occurs in sputum and in secretions from the tonsils, the smegma bacillus may be mistaken for the tubercle bacillus unless care is used in differentiation.

In 1884, Lustgarten, who discovered *Bacillus smegmatis*, believed it to be the cause of syphilis. Subsequent studies, however, discredited this assumption, for *B. smegmatis* was found to occur upon the genitals of healthy as well as diseased individuals. Little significance attaches to this micro-organism, since the smegma bacillus is found as a harmless saprophyte in the mucous membranes of the genitals in individuals who are not diseased.

from the nose and throat. The contagiousness of leprosy is a moot point. Physicians and nurses using sanitary precautions rarely contract the disease, which indicates that leprosy is far less contagious than many other microbial diseases. Nevertheless, as with tuberculosis, there is contradictory evidence on this point. The following striking example was reported by Sticker: A girl living in Holstefershof, where no leprosy existed, married in 1860 and went to another town to live with her mother-in-law, who was a leper. She remained healthy herself, but her three children became leprous. Her younger sister came to her house and slept with the children. After returning to her native town, Holstefershof, the younger sister developed leprosy. The daughter of the younger sister married a man fifty-two years of age. He acquired leprosy. Further, a tailor and his wife, who came from a place where no leprosy existed, were frequent visitors at the latter household. Both contracted the disease. Thus the mother-in-law who was leprous must be considered the original source of infection for eight individuals who acquired the disease.

No case of leprosy can be found in which careful examination of the past history will not reveal direct contact with a previous case, according to Hansen, who discovered the leprosy bacillus. There comes to mind the martyrdom of Father Damien, who contracted the disease while caring for the lepers of the Sandwich Islands, and similarly of Father Boglioli in New Orleans. Not infrequently the incubation period — that is, the period of time which elapses between exposure to infection and the onset of symptoms — may be very protracted in leprosy. The author was recently told about a man who visited an island where leprosy was known to exist and then returned to his native town in Massachusetts. Seven years afterwards he developed leprosy.

There is more than a ray of hope for the successful treatment of leprosy. Chaulmoogra oil, which is derived from the seeds of certain plants, appears to be of value in the treatment of leprosy. While it is too early to conclude that the problem has been solved, nevertheless, by certain refined methods of preparation, there is every reason to believe that chaulmoogra oil will prove therapeutically effective.

A leprosy-like disease has been described among rats, and is

known as rat leprosy.[1] "A peculiar feature of its distribution is the fact that in San Francisco as the writer [Zinsser] was told by McCoy, almost all the rats that suffered from this disease came from the district in which the retail meat business is located, known as 'Butchertown.'"

[1] A microbe closely allied to *Bacillus lepræ* is the bacillus of Johne's disease, chronic enteritis, or paratubercular dysentery of cattle, which is comparatively common in this country.

Chapter X

THE TYPHOID-DYSENTERY-COLON GROUP

I. TYPHOID FEVER

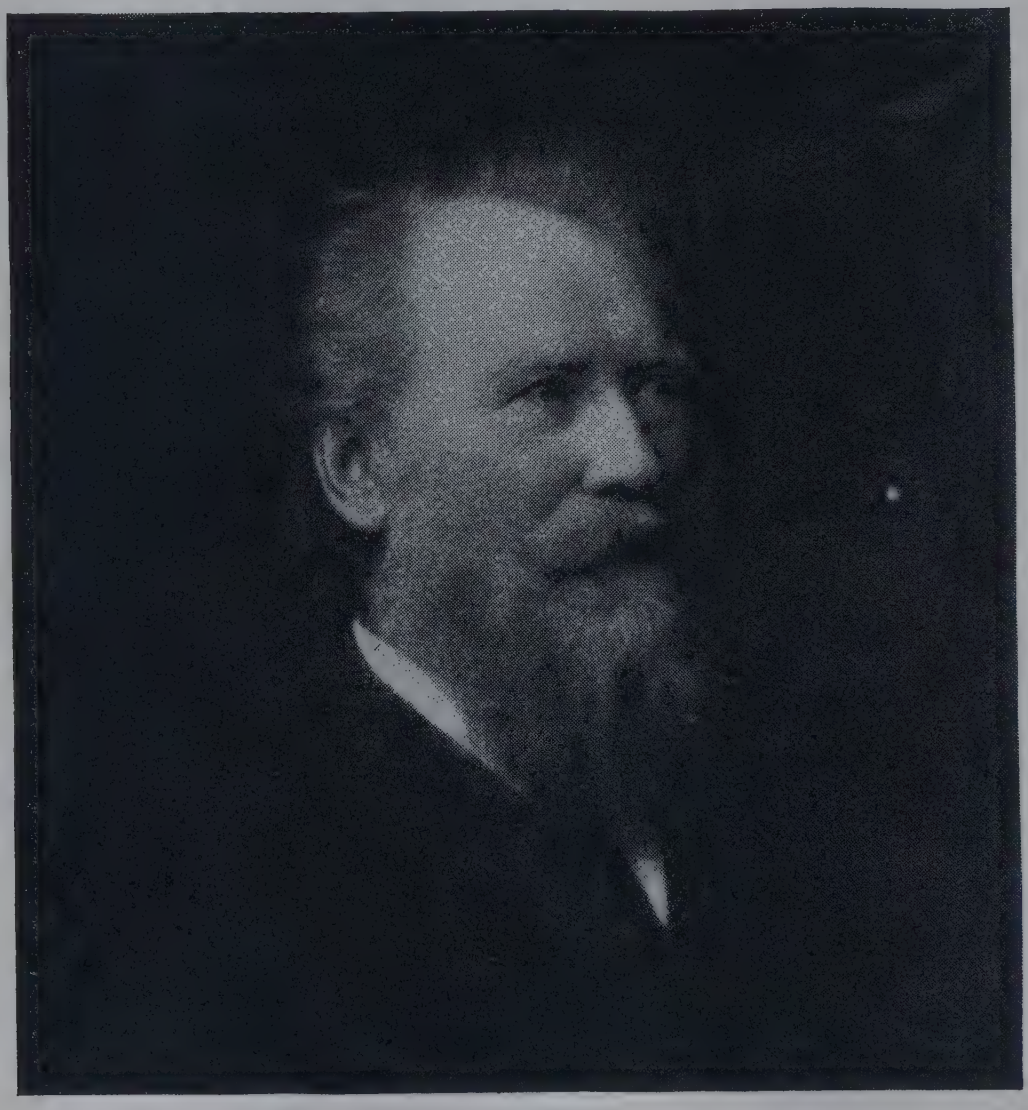


Figure 54

Eberth, discoverer of the cause of typhoid fever.
(After Deschiens.)

Few microbial diseases have been conquered so completely by modern sanitation as has typhoid fever. In fact, the purity of water and ice, the control of milk, and the disposal of garbage and sewage in any community are in direct relation to its freedom from typhoid fever. Strange to say, the principal cities of Europe

have a better record in this respect than those of the United States.

In any general community typhoid fever is more likely to prove fatal to infants and adults than to children. Diagnosis of this disease in infants is naturally beset with difficulty in the early stages, since many of the symptoms resemble those of other diseases. Attention should be directed at once to the milk-supply. Often this lead strikes the mark — sometimes it proves only baffling. Thus, as reported by Morse, a child falls ill in one section of a large city while an epidemic of typhoid fever, caused by infected milk, ravages another part of town. The milk which he drinks is bought at a store in his own neighbourhood, the proprietor of which asserts that none of his milk comes from dealers in the typhoid-infected district. The child has not been away from home and there is no typhoid fever in his district. Neither his milk nor his water is boiled. Perhaps he vomits a few times. His appetite becomes feeble, and for several days he has two to three green stools, containing considerable mucus. Fever follows. He is drowsy most of the time and coughs occasionally. He has a slight bronchitis. The spleen is enlarged. There is a slight rash on the abdomen. These findings, together with the fever and drowsiness, indicate typhoid fever.

FIGURE 55

Typhoid-fever bacilli.
(After Conn and Conn.)

The infectious nature of typhoid fever has long been recognized. Eberth (see fig. 54) in 1880 was the first to describe *Bacillus typhosus*, which Gaffky proved was the specific cause of this disease. The bacillus of typhoid fever is a short, rather plump rod, with rounded ends. (See fig. 55.) Unlike the diphtheria, tubercle, and other bacilli previously described, this bacillus is motile by virtue of twelve or more flagella, peripherally arranged. It is easily stained with ordinary dyes and is Gram-negative. It is readily grown on common laboratory media and has a characteristic delicate glistening appearance on potato. The chief method of differentiating typhoid fever from the closely related dysentery and colon bacilli, aside from serologic tests, is by growth on various sugars. The typhoid-fever bacillus forms neither acid not gas

when milk sugar (lactose) is present. Not all typhoid bacilli are alike, however, for some ferment xylose (a sugar) rapidly, others slowly. As has been suggested, it would seem more appropriate to make obsolete the term "typhoid bacillus" in favour of a typhoid group of bacilli. Often *Bacillus fæcalis alcaligenes*, which is commonly found in the normal intestinal tract and only infrequently produces disease, is mistaken for some member of the typhoid group.

Like most parasitic bacteria, typhoid bacilli grow best at human body temperature. Temperatures from 59°F. to 106°F., however, permit growth. With an adequate supply of moisture typhoid bacilli may remain alive for months or even years. "In carefully sealed agar tubes Hiss found the organisms alive after thirteen years" (Zinsser). They may remain alive for over a month in natural waters or for more than three months in ice. As might therefore be expected, they are somewhat more resistant to ordinary disinfectants than a number of other non-spore-forming bacteria.

Typhoid bacilli invade the human body via the mouth, through the agency of infected food, water, milk, ice, or fingers which have come in contact with infected materials, directly or even indirectly. They seem to have a predilection for the intestines, where they multiply and cause inflammation, particularly in the lymph nodules. Thence they are distributed by the blood-stream and may set up secondary local inflammatory processes in the liver, gall-bladder, spleen, or other parts of the body. It is still a question whether the symptoms of typhoid fever, which include headache, fever, chills, vomiting, etc., result from a destruction of intestinal or other tissues by the bacilli, or, as is more reasonable to suppose, from a poisoning of the system by the non-soluble toxin, or poison, elaborated within the typhoid bacilli themselves.

Compared with many other infections, typhoid fever is a much more general disease, in that the toxin affects all the organs of the body, even though the infectious process itself is generally localized in the intestinal tract. The complications of typhoid fever, such as typhoid meningitis, typhoid pneumonia, typhoid skin and liver abscesses, are greatly to be feared, for they often terminate fatally.

Bacteriologic culture of the blood of patients in the first week of the disease almost invariably reveals the presence of typhoid bacilli. They may also be found after careful search in a certain proportion of urinary and fæcal excretions. These tests are of value in diagnosing doubtful cases and in tracing "carriers" of these bacilli. The most widely known single test for typhoid is

FIGURE 56

Widal test for typhoid fever. Above, normal typhoid bacilli (at the right, top view; at the left, cross-section). Below, typhoid-fever bacilli clumped or agglutinated by patient's serum. (After Park, Williams, and Krumwiede.)

the Widal test. It is carried out in the following manner: A small amount of the patient's blood is sent to a laboratory. Several definite dilutions of blood-serum are made and a drop of each is mixed with a drop of known *Bacillus typhosus* culture upon a cover-slip, which is inverted over a hollow slide and examined microscopically. (This is the "hanging-drop" method described on page 44.) If the reaction is positive, it will be seen that the bacilli, which originally swim about actively, gradually slow down and huddle into small clusters. In an hour or less these clusters become dense concretions, through the process known as agglutination. (See fig. 56.) If clumping occurs within an hour in

a dilution of one part of blood-serum to about fifty parts of physiologic saline it is regarded as definite evidence of typhoid fever in the patient.

While the Widal test is universally used, its value has not wholly met the early hopes of its discoverer. For one thing, it is not sufficiently sensitive to disclose typhoid fever in the first few days of the disease. For another, there are conditions other than typhoid fever which may yield a positive reaction — namely, jaundice and tuberculosis. Finally, the serum from a patient who has been vaccinated against typhoid fever agglutinates because such individuals develop agglutinins as a result of vaccination. Mention should be made of the fact that, in addition to agglutinins, typhoid-fever serums contain precipitins and opsonins, which are agents in the blood of value in fighting harmful bacteria.

The diagnosis of a typical case of typhoid fever in adults usually offers little difficulty — it is the very mild cases that are likely to escape detection. And these are a menace to the health of the community because, like carriers, they can infect others. As with diphtheria, the patient who has once contracted typhoid fever may harbour *Bacillus typhosus* for a long period of time, infecting individuals with whom he comes in contact. During any epidemic the number of carriers is greatly increased because of the widespread dissemination of the bacilli. The principal sites, or foci, in which the bacilli persist are: intestine, gall-bladder, and liver. The typhoid carrier, incidentally, not infrequently develops gall-stones. When this occurs it is difficult to cure a typhoid carrier by means other than the surgical removal of the gall-bladder. This is true despite the use of vaccines, or drugs such as urotropin (a common urinary antiseptic). Curiously, persons who have had typhoid fever are sometimes healthier after the disease than they were before. And those who were thin before typhoid fever are likely to become stouter, not only immediately following the disease, but throughout the remainder of their lives.

Modern sanitary methods have done much to safeguard man against typhoid fever, but the sources of danger are more numerous and difficult to control than might ordinarily be supposed. First to be considered is the water-supply. Drinking-water be-

comes polluted with typhoid bacilli, directly or indirectly, by excreta from typhoid-fever patients, or articles contaminated by them. Consequently, if all excreta are not immediately disinfected, rain or snow wash the bacilli down into the soil, whence they seep into the water-supply. Worse, the water-supply may be polluted by permitting sewage, garbage, or similarly contaminated substances to enter it directly. Nowadays, with sanitary supervision and purification of water by chlorine gas and other antiseptics, danger of typhoid infection has been greatly diminished in the larger cities. Nevertheless, some of the bathing-beaches around even such a metropolis as New York have been recently condemned as unfit because of contamination by sewage and garbage. Formerly three out of every four epidemics of typhoid were attributable to polluted water. The problem still persists in rural districts where well-water is used extensively. Not only is a purification plant essential to safeguard the water-supply, but it is fully as important that it function perfectly. Any temporary defect may start an epidemic. Many such instances are on record. Not long ago an epidemic of typhoid was reported in California following the pumping of water directly from the river into the mains without purification for a single day. This was because of repairs in progress at the plant.

Milk, next to water, is probably the most frequent source of typhoid epidemics. Running water tends to purify itself. Milk, on the other hand, is an excellent source of food for typhoid bacilli. This means rapid multiplication of these harmful bacteria. Milk moreover, is readily contaminated with typhoid germs by handlers who are carriers, or by bottles returned from houses where typhoid fever or typhoid carriers exist.

Oysters, when fattened for the market by floating in sewage, according to common practice, are a menace. The recent typhoid epidemics of New York and Chicago have been traced to this source. Similarly, after a Yale University alumni reunion at New Haven, twenty-five of the celebraters had to wind up in the hospital, stricken with typhoid fever. Unless the water in which the oysters are grown is free from pollution, it is obvious that oysters may carry typhoid bacilli. Similarly, uncooked vegetables, particularly lettuce, radishes, etc., may prove a source of infection. Often these vegetables are grown in soil the underground

waters of which are polluted with sewage. Thorough washing of vegetables and fruits eaten in the uncooked state, therefore, is a prerequisite to freedom from infection.

Ice as another source of typhoid bacilli is frequently either underestimated or exaggerated. Typhoid bacilli are found in the waters from which ice is made. Thus, the Hudson River, which supplies about four-fifths of New York's ice, harbours typhoid bacilli. But, as Park, Williams, and Krumwiede have pointed out, there is no increase in the incidence of typhoid fever during the months of March, April, and June such as would be expected when ice is placed in drinking-water or in other beverages. This means that freezing kills off the germs. The longer ice is stored, moreover, the smaller are its bacterial numbers, so that after four weeks' storage there is as little danger from typhoid as when water is filtered through sand. The top layers of freshly cut ice, however, do contain an appreciable number of bacteria and must therefore be considered unsafe for public consumption.

Flies and insects are important agents in carrying typhoid bacilli from excreta or garbage to the domicile, alighting on food and forthwith contaminating it. Infection from this source is particularly to be expected in camps, especially during war time, or in rural districts where open latrines are still in use. They should be continually disinfected with chloride of lime or some other suitable chemical.

The increased attention which is being paid to the sanitary supervision of water, milk, ice, and other food-supplies has done much to reduce the incidence of typhoid from these sources. Communal activities directed against the spread of disease place more responsibility than ever upon the individual; for infection by direct contact appears to be the cause of typhoid fever in a majority of cases. Direct contact need not necessarily be with a typhoid patient. A typhoid carrier may serve equally well in spreading the disease. For this reason the rigid examination of all persons connected with the handling of food is of supreme importance. A single carrier alone may start an epidemic.

Witness the case of the notorious "Typhoid Mary." In 1901 a visitor in the family in which "Typhoid Mary" was cook developed typhoid fever. One month after taking a new position, the laundress of the new household contracted typhoid. Two

weeks after the arrival of "Typhoid Mary" in a new position, a laundress contracted the disease, and soon seven members of the household were sick. Two years later "Typhoid Mary" went to a home on Long Island. Within three weeks of her appearance on the scene, four servants had typhoid. Again two years later, in a new position, six out of eleven persons in the house came down with typhoid. Less than three weeks later she took another position, and the laundress contracted typhoid. In 1907, two months after entering a household in New York City, two cases of typhoid fever developed, one of which proved fatal. Let us quote Park, Williams, and Krumwiede directly on the further activities of "Typhoid Mary":

"The cook was removed to the hospital March 19, 1907. Cultures taken every few days showed bacilli off and on for three years. Sometimes the stools contained enormous numbers of typhoid bacilli and again for days none could be found. She was released on parole in 1910 promising to report to the Health Department and not to engage in cooking. She broke her parole and disappeared. In 1915, in an epidemic of typhoid at a maternity hospital, a total of twenty-five cases developed. Investigation showed that food infection was the cause and the cook was identified as 'Typhoid Mary.' During the period of disappearance she infected a friend and was the cause of several cases in a small private sanatorium and of twenty-seven cases in a maternity hospital. Since then she has again been isolated. She is known to have been the cause of at least fifty cases of typhoid fever. We recently traced some hundreds of cases of typhoid fever to a milk supply produced at a farm, looked after by a typhoid carrier who had typhoid fever forty-seven years ago."

The prevention of typhoid fever has never attained the satisfactory status of diphtheria prevention and treatment, chiefly because no soluble toxin has been isolated from *Bacillus typhosus*. Various vaccines and serums have been prepared for the specific treatment of typhoid fever. Promising though some of them are, none has as yet attained complete success. Nevertheless, a valuable method for the *prevention* of typhoid was devised by Wright in 1896. It consists in the injection of a culture of typhoid bacilli killed by heat. Typhoid vaccination has been compulsory in the United States Army since 1910. In 1913 there was only one case

of typhoid in over eight thousand men. Improved methods since Wright's discovery have served to lower the incidence of typhoid and in consequence have lowered the mortality from this disease, as evidenced by statistics of the World War compared with those of previous wars.

Typhoid-fever cases during the first year of the Civil War were at the astounding rate of 710 per 1000, with a death-rate of 200. During the Spanish-American War of 1898, which was in the days before vaccination, the rate was 142 per 1000, with a death-rate of 14. But in the World War four million men passed through the American camps and only 0.37 per 1000 contracted typhoid fever, thanks to the use of "triple vaccine," which included typhoid and paratyphoid A and B (to be described presently). This represents a tremendous reduction in illness and death compared with previous wars. Furthermore, the value of compulsory universal typhoid vaccination for armies is clearly demonstrated by the superiority of the United States over all other countries in the low incidence of typhoid fever during the World War. The French, the Italian, and even the German Armies all had relatively more cases of typhoid fever than the American Army because none of the foreign armies were so thoroughly protected against the disease by vaccination. To be sure, allowance must be made for the fact that the foreign armies rushed headlong into war, while the American Army had an opportunity to become prepared — at least from a medical standpoint. "In Europe," to quote Zinsser, "in spite of the most terrific sanitary conditions in some of the battlefields during the summer, and with perhaps ten million troops in France, there were only 488 cases with 88 deaths, and this, in spite of the fact, as we, ourselves, observed, that the opportunities for transmission were enormous in battle areas in which sanitation was practically impossible, and water supplies were bad and could not be corrected. The question still remains as to how long typhoid vaccination can be regarded as efficient. There is no absolute information upon which opinions can be based. Vaccination is not a complete protection at any time, and a recently vaccinated individual may still occasionally contract the disease if he is injected with a large dose of virulent organisms. The protection, however, is very powerful and will prevent contraction of the disease from the ordinary chance

infection. We should state on general information that repetition every two years ought to be sufficient for civilian purposes."

2. PARATYPHOID AND MEAT-POISONING

While typhoid fever is caused by *Bacillus typhosus*, there are several other closely allied bacilli which produce similar symptoms — namely, those belonging to the groups known as "paratyphoid A and B." Mild fever as a rule results from infection by bacilli of the paratyphoid A group, and the incidence is relatively low in the temperate regions. In form and staining the paratyphoid bacilli are identical with the typhoid-fever bacillus. There are however, certain fermentation and serologic criteria valuable for differentiation, as indicated below.[1]

The typhoid-like bacilli constitute a large group, the members of which cause meat- or food-poisoning. The *enteritidis* group particularly is responsible for epidemics following the ingestion

[1] Composite Table of Most Important Types (after Zinsser).

Bacillus	*Dextrose*	*Mannite*	*Maltose*	*Lactose*	*Xylose*	*Rhamnose*	*Saccharose*	*Dulcite*	*Lead acetate agar*	*Motility*
B. coli communis	(+)	(+)	(+)	(+)	×	×	−	(+)	varies	+
B. coli communior	(+)	(+)	(+)	(+)	×	×	(+)	(+)	varies	+
B. acidi lactici	(+)	(+)	(+)	(+)	×	×	−	−	...	+
B. lactis ærogenes	(+)	(+)	(+)	(+)	×	×	(+)	−	...	+
B. paratyphosus "A"	(+)	(+)	(+)	−	−	+	−	slow	−	+
B. paratyphosus "B"	(+)	(+)	...	−	+	+	−	+	+	+
B. enteritidis	(+)	(+)	...	−	+	+	−	+	+	+
B. abortus	(+)	(+)	...	−	+	+	−	+	−	+
B. of hog-cholera	(+)	(+)	...	−	+	+	−	irreg.	−	+
B. typhi murium	(+)	(+)	...	−	+	+	−	+	+	+
B. typhosus	+	+	+	−	slow	−	−	slow	+	+
B. dysenteriæ Shiga	+	−	−	−	×	×	−	−	×	−
B. dysenteriæ Flexner	+	+	+	−	×	×	−	−	?×	−
B. dysenteriæ "Y" (Hiss-Park)	+	+	−	−	×	×	−	×	×	−
B. dysenteriæ Strong	+	+	−	−	×	×	+	×	×	−
B. fæcalis alcaligenes	−	×	×	×	×	×	×	×	×	+
B. morgani, No. 1	(+)+ slight gas	−	−	−	?	?	−	−	?×	+

Legend:

(+) = acid and gas
\+ = acid, no gas
− = negative
× = not needed for identification

of infected meat or edible organs of cattle. Thus, Gärtner discovered *Bacillus enteritidis* in an epidemic of meat-poisoning in a Saxony village in 1888. Fifty-seven persons who had eaten the flesh of a diseased cow became ill. A young man who had eaten almost two pounds of the raw meat died in about thirty-five hours. What a lesson to gluttons! From the organs of this individual, *Bacillus enteritidis* was isolated. The same bacillus was found in the diseased cow the meat of which he had eaten. Similar outbreaks of meat-poisoning have been reported from other countries.[1]

3. DYSENTERY

Dysentery is practically synonymous with diarrhœa and is a clinical term applied to a variety of acute and chronic diarrhœal conditions which are accompanied by bloody stools and some degree of abdominal pain. But not all diarrhœas are due to true dysentery. There are many dysenteries caused by different microbes — bacteria as well as protozoa. It was a Japanese bacteriologist, Shiga, who discovered the bacillus responsible for the dysentery epidemic in 1898.

Other investigators have since isolated similar bacilli, so that they have been conveniently designated as the dysentery group of bacilli. They are responsible for most of the dysentery occurring in temperate regions and for much of the dysentery occurring in the tropics. Flies are undoubtedly active agents in the dissemination of the dysentery bacilli. Where sewage and garbage are not properly disposed of, flies alight on refuse or excreta and then infect food intended for human consumption. The dysentery epidemics of the American Army in 1918 have been ascribed by Zinsser to this source. Transmission from man to man directly and indirectly through contamination is also an important consideration in epidemics of dysentery. As in typhoid fever, there are healthy and convalescent carriers of dysentery bacilli.

Furthermore, the dysentery bacilli resemble the typhoid

[1] Bacilli closely resembling those of the *enteritidis* group infect swine (hog-cholera group), fowl (*B. pullorum; B. sanguinarium*), mice (*B. typhi murium*), parrots (*B. psittacosis*), guinea-pigs (*B. pestis caviæ*), and rats (Danysz type); and cause infectious abortion in horses (*B. abortus equi*). The table on page 125 gives the chief cultural differences between them as determined by laboratory examination.

group both in form and in staining. (See fig. 57.) But the dysentery bacilli possess little or no motility; and, as might be expected flagella, which are the bacterial organs of locomotion, have not been observed. The dysentery group is large and the chief differences between the various members are to be found in their fermentation and serologic properties, which also distinguish them from the typhoid bacilli. A number of bacilli from the stools of infants suffering from diarrhœa (first isolated by Morgan) also resemble the paratyphoid-dysentery group, but the Morgan bacilli are not regarded as having the same disease-producing powers (see page 125).

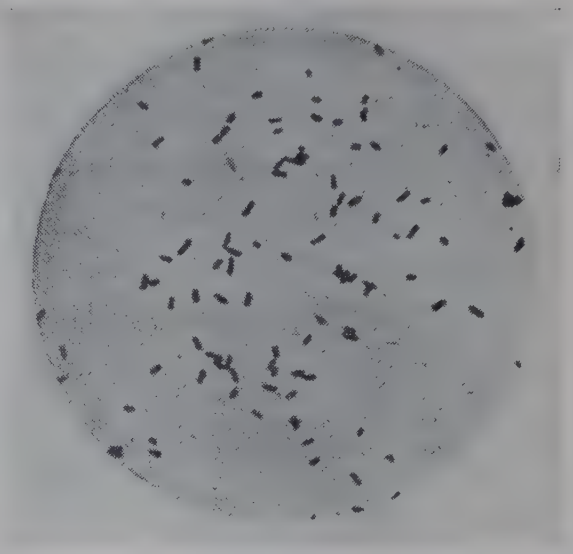


FIGURE 57

Dysentery bacilli. (After Jordan.)

In the human body, dysentery bacilli are to be found only in the intestines; consequently excreta are as dangerous in spreading this disease as in typhoid fever. Serum treatment has been attempted for dysentery, Shiga and others having reported encouraging results. But these seem most favourable when dysentery bacilli of the Shiga type, which produce a soluble toxin, as do the diphtheria bacilli, are involved. Bismuth in large doses is of value in treatment.

FIGURE 58

Colon bacilli (magnified 1100 times). (After Park, Williams, and Krumwiede.)

4. COLON BACILLI

The term "typhoid-dysentery-colon group," designates the whole range of closely related plump, Gram-negative rods comprising the groups mentioned (typhoid, paratyphoid, *enteritidis*, dysentery, etc.), as well as the colon bacilli, typified by *Bacillus coli*. (See fig. 58.) The latter

was found in the stools of a breast-fed infant by Escherich in 1886. Colon bacilli, among which are included *Bacillus lactis ærogenes* and *Bacillus acidi lactici*, commonly found in milk, are widely distributed in nature. They may be isolated from the air, from water, from the soil, but most abundantly from the intestinal tract of man and the higher animals. Again, the principal method of differentiation among members of the colon group as well as from other groups lies in sugar fermentation (see table and fig. 59).

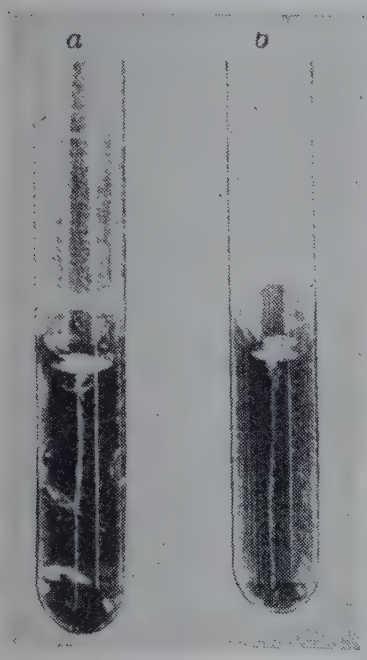


FIGURE 59

Colon bacilli, showing gas bubbles in agar containing sugar (at the left). Typhoid-fever bacilli, showing no gas production (at the right.) (After Jordan.)

Under ordinary circumstances *Bacillus coli* must be regarded as a harmless organism in the intestinal tract of man, just as it leads a saprophytic existence in nature. Nevertheless, it possesses striking disease-producing potentialities. Thus a large number of kidney, bladder, and gall-bladder infections are caused by *Bacillus coli*. In fact, some investigators consider it responsible for four out of every five cases of infection of the urinary tract. Treatment for such infections usually consists in the administration of a urinary antiseptic, such as urotropin or hexylresorcinol.

Interest in the colon group of bacilli as it occurs in nature centres on its value in indicating the purity of the water-supply. While the colon bacilli are themselves innocuous when ingested, nevertheless their presence in water is in direct ratio to the numbers of disease-producing organisms of the typhoid and paratyphoid groups. Consequently, the number of *B. coli* present in water is an index of its purity or pollution. There are many bacilli which resemble those of the colon-typhoid group, and among them are the members of the Proteus group, widely distributed in nature as saprophytes and important in the breaking down of proteins. *Bacillus proteus vulgaris* (see fig. 60), typical of this group, differs from the colon-typhoid bacilli in that it liquefies gelatin. A common organism in sewage is *Bacillus cloacæ*, which does not belong to the Proteus group, but is closely related to it. Mention may here be made of *Bacillus pyo-*

cyaneus (see fig. 61), the short bacillus of blue and green pus, which does not ordinarily produce disease in man, but may under certain circumstances — such as general run-down condition, especially in children — become a dangerous source of infection. When grown artificially on a solid medium it produces a characteristic greenish hue.

Finally, in a discussion of short Gram-negative bacilli the members of the Friedländer group, previously mentioned in connexion with pneumonia, should be included. The Friedländer bacillus, otherwise known as "*Bacillus mucosus capsulatus*," is a

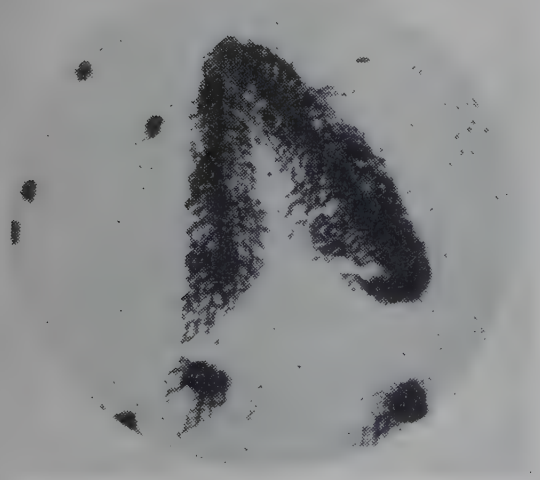


FIGURE 60

Bacillus proteus (*showing numerous flagella*). (*After Jordan.*)

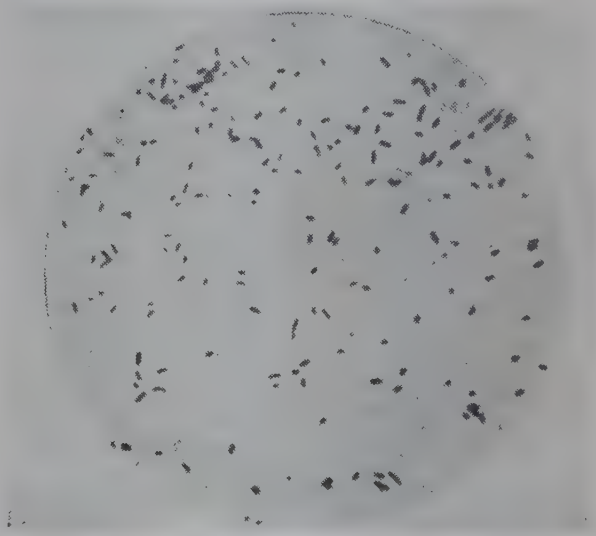


FIGURE 61

Bacillus pyocyaneus. (*After Jordan.*)

short, thick capsulated rod, first described as a coccus, which Friedländer erroneously considered to be the cause of lobar pneumonia. Rather it is an incitant to nasal catarrh, sinusitis, and similar conditions. A closely related rod is the bacillus of rhinoscleroma, which produces granular inflammation in and about the mouth, nose, and throat. While this infection is rare in America, it occurs often in south-eastern Europe. *Bacillus ozænæ* (see fig. 62), which causes fetid nasal catarrh, is indistinguishable from *Bacillus mucosus capsulatus*.[1]

In the colon-typhoid-dysentery group we are dealing with a host of closely related bacilli. Many are essentially pathogenic (disease-producing); others primarily saprophytic (harmless),

[1] Ozæna, according to Perez, may be caused by another similarly capsulated rod, known as the "Perez bacillus of ozæna."

with disease-producing potentialities. All possess certain characteristics which make differentiation a difficult task. Their common properties are: (1) similar form (short, rather plump, non-spore-bearing rods); (2) Gram-negativeness when stained; (3) similar growth on agar and gelatin; (4) inability to liquefy gelatin.

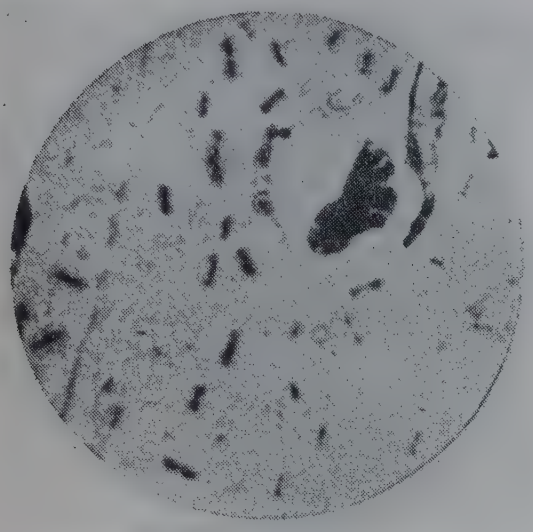


FIGURE 62

Bacillus ozænæ (*showing capsules surrounding pairs of bacilli*). (*After Jordan.*)

Much bacteriologic investigation has been expended on this group of organisms, and much research must yet be done before satisfactory subdivisions are finally established. To date, the best criteria have been the fermentation of various sugars and serologic tests. Nor is this purely academic research, for upon its application depend the health and life of communities the world over.

Chapter XI

INTESTINAL BACTERIA

Not all bacteria in the human intestinal tract are harmful. In the preceding chapter, although emphasis fell upon the bacilli causing typhoid fever and dysentery, a number of saprophytes normally inhabiting the intestinal tract were discussed. To judge from the millions of bacteria in adult excreta, one would never suspect that the human intestinal tract is sterile at birth. Yet it is believed to be so. Within twenty-four hours after birth, however, a number of adventitious organisms gain entrance into the intestinal tract, and from then on, the flora or bacteriologic population grows more numerous and complex with increasing years. Many factors, such as diet, drugs, disease, etc., play determining rôles.

Figure 63

Bacillus bifidus (magnified 1800 times), showing forked or bifid branching. (After Park, Williams, and Krumwiede.)

Healthy breast-fed babies after the first few days of feeding yield a characteristic long, thin, Gram-positive bacillus named "*Bacillus bifidus*," because of its forked or bifid ends. (See fig. 63.) This bacillus, intensively studied by Tissier, lives only in the absence of free oxygen (obligate anaerobe). It ferments milk sugar (lactose) to form lactic acid, but not gas. The formation of lactic acid in the baby's intestinal tract makes life unpleasant for other less desirable putrefactive bacteria and thereby safeguards the nursling. The artificially fed infant, who has to forego the benefits of mother's milk, has few if any of these organisms, but harbours a protective bacillus closely allied to *Bacillus bifidus* — namely, *Bacillus acidophilus*. The latter also forms lactic acid from lactose without the production of gas. In addition to *Bacillus acidophilus*, one finds in the stools of

artificially fed infants members of the colon group of bacilli and other harmless and normal inhabitants.[1]

During childhood and through adolescence the bacterial flora usually become predominantly colonic in type, with a larger variety of organisms than are to be found in infancy. In other words the control over the nursling's intestinal flora exerted by the lactic acid formed by *Bacillus bifidus* or *Bacillus acidophilus* from milk sugar is lost by the introduction of complex, highly nitrogenous foods. In consequence, the Gram-negative putrefactive bacilli gain the ascendency. Constipation or diarrhœa may follow.

There are two methods whereby we strive for a return to the simple, predominantly Gram-positive flora of our earliest days. One method is to regulate the diet. The other is to introduce large numbers of the protective lactobacilli (as *Bacillus bifidus* and *Bacillus acidophilus* are now called). There is still a third method, by far the most popular, but most to be deplored — namely, the continual use of cathartics. The proper regulation of the diet, together with accessory hygienic measures, belongs to the domain of the gastro-enterologist rather than the bacteriologist, the latter being better able to assist in promoting the second method — namely, the purposeful alteration of the intestinal flora by the use of suitable cultures.

Long before the science of bacteriology was conceived, the tribes of Asia, Africa, and Europe placed much faith in the use of milk soured by chance exposure to the atmosphere. The genial microbes, all-unrecognized, produced such present-day soda-fountain delicacies as koumiss, matzoon, yoghurt, and the like. These sour-milk beverages, originated by chance, were later perpetuated by design, merely by transferring portions of the soured milk to fresh sweet milk. Metchnikoff, the great Russian bacteriologist of the Pasteur Institute, attributed the health and long life of the Bulgarian peasants to their custom of drinking large quantities of yoghurt, or milk soured by another lactobacillus, appropriately called "*bulgaricus*." His plan, therefore, for disposing of human ills — a majority of which he believed originated in the intestinal tract — and to prolong life was to replace

[1] Enterococci and members of the *Bacillus mesentericus* group (large, motile, spore-bearing rods).

the harmful putrefactive bacilli by the protective lactobacilli. The theory was sound, but the practice unhappy. In order to transform the intestinal flora from a harmful to a beneficial type it is obviously essential that the desirable lactobacilli introduced for that purpose remain alive and active in the human intestine. But recent investigation has shown that such is not the case when *L. bulgaricus* (*L.* being the abbreviation for *Lactobacillus*) is ingested. In a word, the failure of this microbe to survive in the intestine dealt a death-blow to its popularity.

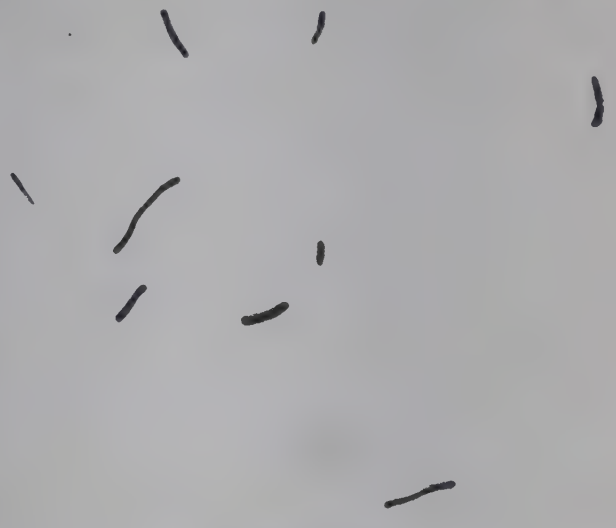


FIGURE 64
Lactobacillus acidophilus.

Out of the ashes rose the phœnix — *L. acidophilus*. Twin brother to *bulgaricus*, it is identical in appearance and similar in most of its characteristics. (See fig. 64.) Both are large, Gram-positive rods, usually in long chains. On solid media they form characteristic colonies, which look like specks of wool. (See fig. 65.) They coagulate milk, fermenting the milk sugar to lactic acid, which gives it a pleasantly sour taste. Most strains of *L. acidophilus* ferment maltose (a sugar). Most *L. bulgaricus* strains do not. But there is an all-important distinction between *L. acidophilus* and *L. bulgaricus:* the former survives in the human intestine; the latter does not.

FIGURE 65
A single colony of lactobacillus acidophilus.

When ingested in sufficient numbers, *L. acidophilus* is capable

of inducing the transformation of the intestinal flora which Metchnikoff so much desired. For a detailed discussion of the value of *L. acidophilus* the interested reader may consult the author's *Lactobacillus Acidophilus*. Suffice it to say, milk soured by this bacillus has proved effective in the treatment of a number of intestinal disorders, chief of which are constipation and diarrhœa. (See fig. 66.) Patients who before treatment had averaged one normal defecation per week or less, when given one quart of acidophilus milk per day for about a month, have normal defecations almost every day. A transformation of the flora to a predominantly Gram-positive type is noted as a result of the

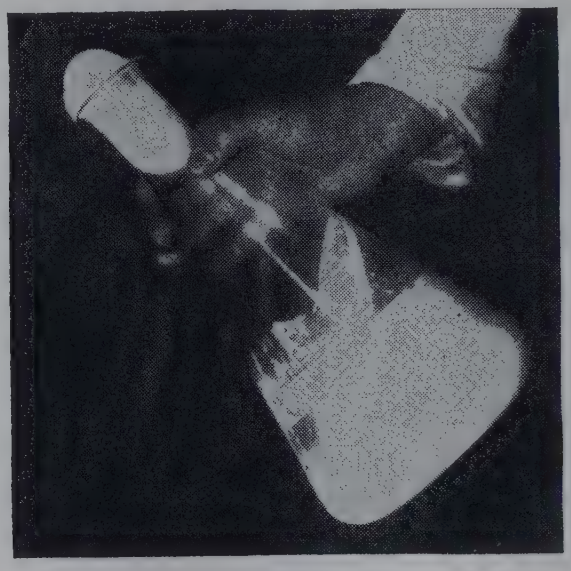


FIGURE 66

Flask of acidophilus milk, showing smooth homogeneous character of the curd.

bacteriologic analyses of fæcal specimens. Lactose (milk sugar) is a valuable adjunct to acidophilus therapy, since it furnishes a source of food to the acidophilus bacilli in the lower intestine. Lactose alone or in combination with other sugars, however, cannot accomplish in the same time the results obtained by the administration of large numbers of living *L. acidophilus* organisms. A majority of patients who had benefited during treatment with acidophilus milk find that benefits persist even after treatment is discontinued.

There are now a number of different kinds of acidophilus products on the market, ranging the gamut from acidophilus milk, through broths, fruit juices, and emulsions, down to tablets and candies. The quality of most of these products has recently

been improved, yet there are few which approach laboratory-made acidophilus milk in actual count of living organisms. The layman cannot judge the value of an acidophilus product, nor can a physician ordinarily without the help of expert bacteriologic opinion. This means that acidophilus therapy must reach the public in a gradual manner. Worthless preparations are a waste of time and money. Entirely satisfactory preparations have still to be offered.

In conclusion, a word may be said in behalf of our friends the microbes of the intestinal tract. "Microbe" is a term which conjures up a picture of infectious disease, and rightly so, because of what bacteriology has done for medicine. Most of the microbes brought to our attention are our foes. But a few, such as those just mentioned and others which are of importance in agriculture and industry, are our friends. They merit recognition.

Chapter XII

LOCKJAW (TETANUS), BOTULISM, WOUND INFECTIONS, ETC.

I. LOCKJAW (TETANUS)

Just as human beings might be arbitrarily classified in two groups — those breathing through the nose, and those breathing through the mouth — so bacteria are classified according to their requirements of free oxygen. With few exceptions, the microbes described in the foregoing chapters (aerobes) require free oxygen for their development. But the anaerobes, which grow best in the absence of free oxygen, are also an important group in the production of infectious disease and deserve special consideration.

Although lockjaw, or tetanus, has been known through the centuries in all parts of the world, its incidence is comparatively low. The symptoms of the disease, however, are spectacular and horrible. Chief among them is a spasm of the muscles of the jaw and neck giving the mouth a characteristic tense expression, a fixed sardonic grin. "These spasms, in severe cases, may involve the trunk, back, and diaphragm. The paroxysms are associated with agonizing pain and the patient may be held as in a vice, unable to utter a word. Usually he is bathed in a profuse sweat" (Osler). Death comes during a paroxysm as a result of heart-failure or asphyxiation, the latter due to paralysis of the diaphragm. Until recently the mortality rate in tetanus was very high, especially among children. It was common knowledge that for many years half of the deaths of new-born Negro children in the West Indies were due to this disease. St. Kilda for example, has been scourged by the "eight days' sickness among the new-born." "Of 125 children, 84 died within 14 days of birth," according to Osler. In past centuries military campaigns furnished many fatalities from this disease, following wounds. It is particularly interesting to note in this connexion that savage peoples, such as those which inhabited the New Hebrides, poisoned their arrow-heads by

infecting them with tetanus bacilli taken from dirt in crab holes in the swamps.

The infectious origin of tetanus was long suspected, but it remained for a Japanese, Kitasato, to describe the causative microbe, *Bacillus tetani* (1889). It is an anaerobic,[1] slender, Gram-positive, moderately motile rod with numerous surrounding flagella. Large round spores are formed at one end, giving the organism a characteristic drumstick appearance. (See fig. 67.) These spores are extremely resistant to deleterious influences, such as drying or heat, which accounts for the widespread persistence of the organism in nature. One investigator, Henrijean, was able to grow tetanus bacilli from a splinter of wood eleven years after it had caused tetanus in an animal. *Bacillus tetani* is a common inhabitant of soil, manure piles, and dust. It occurs in larger numbers in some localities than in others. Certain sections of Long Island and New Jersey, for example, have become notorious on this account. New York City boasts a fair population of tetanus bacilli.

FIGURE 67

Tetanus (lockjaw) bacilli. (After Conn and Conn.)

Bacillus tetani, like the diphtheria bacillus, excretes a soluble toxin or poison. In fact, this toxin is generally accepted as being the most powerful of the microbial toxins; it is twenty times as poisonous as cobra venom. Tetanus toxin, acting upon the central nervous system of man and domestic animals, produces the symptoms which give lockjaw its horrible name. So drastic is the effect of tetanus toxin upon the nervous system that patients have to be kept in a very quiet, dark room. Any sudden loud noise is often sufficient to initiate violent spasms.

As with diphtheria, animals may be rendered immune from tetanus by receiving injections of gradually increased doses of tetanus toxin. When the animal is able to withstand large doses of tetanus toxin, it is bled and the serum or liquid portion of the blood is used as antitoxin. The chief value of tetanus antitoxin

[1] The organism may be grown readily on ordinary nutrient media, forming colonies that look like fleecy clouds on agar plates from which the supply of free oxygen is cut off. Although it is an anaerobe, it is extremely difficult to make rigid generalizations on this score, for under certain conditions *Bacillus tetani* may even grow well in the presence of free oxygen — as, for instance, in the presence of other microbes. Or, to continue the former insecure analogy, anaerobes increase their oxygen capacity like a mouth-breather who has had his tonsils and adenoids removed.

lies in its use as a preventive against contracting the disease. In all the armies during the World War it was the general practice to inject every man with tetanus antitoxin either before he was wounded or as soon after injury as possible. This routine served to reduce the incidence of tetanus to a negligible figure compared with that in other wars. During the Civil War one soldier out of about every five hundred was infected by tetanus. During the World War, thanks to the use of antitoxin, less than one-tenth of the above incidence was noted — only one soldier out of every 6,224 was infected with *Bacillus tetani*.

Ordinarily the number of cases of tetanus in the United States is low, but after Fourth of July celebrations wounds caused by blank cartridges or other explosives are responsible for the occurrence of many deaths from lockjaw. A truly "safe and sane Fourth" would save many a victim of tetanus from torture and death. The American Medical Association has carried on a vigorous and effective propaganda to this end, and the consequent decline in the mortality rate of tetanus is impressive. Thus, in 1903 there were 406 deaths from tetanus in the United States, the following year 91 deaths, and so on down to 1916, when no deaths from tetanus were reported. Tetanus as a disease, therefore, can be wiped out of civilian life in times of peace and practically eliminated from the battle-field in times of war.

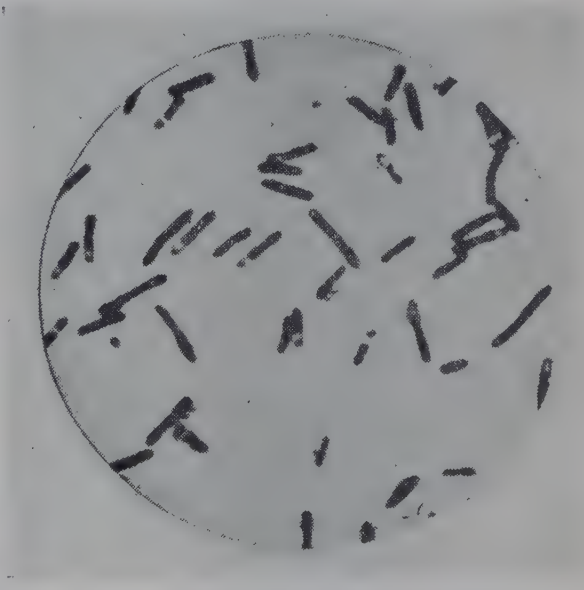
2. BOTULISM

Botulism, or "sausage-poisoning" (from the Latin *botulus*, sausage), is often, though erroneously, confused with meat-poisoning caused by the *enteritidis* group of bacilli already described. Botulism follows the consumption of raw foods such as sausage, salt-fish, etc., or improperly canned foods containing *Bacillus botulinus*. The symptoms of botulism resemble those of atropin poisoning — namely, dryness of the throat, dilation of the pupil with disturbance of vision, deafness, obstinate constipation, retention of urine, disturbance of heart and respiratory action, and absence of fever, often terminating fatally. Botulism is a sudden and dramatic disease, owing to the striking severity of the symptoms.

Bacillus botulinus is a large, slightly motile, Gram-positive, anaerobic rod with oval spores. It grows best at ordinary room

temperature — that is, 65°–77°F. (See fig. 68.) Characteristic spherical, translucent, granular, yellowish-brown colonies are formed in gelatin, which becomes liquefied.

The botulinus bacillus, like that of tetanus and diphtheria, excretes a powerful toxin. Van Ermengem, who first isolated *Bacillus botulinus*, has described several cases of botulism resulting from the ingestion of comparatively small amounts of infected food. Thus in one instance death followed the tasting of a spoonful of spoiled corn; in another case "nibbling a portion of a pod of the spoiled string beans" proved fatal. In general, the mortality rate in botulism is very high. It has been estimated that sixty-four out of every hundred patients contracting the disease succumb.



(*Kolle and Wassermann.*)

FIGURE 68

Bacillus botulinus, the cause of botulinus (showing spores). (After Jordan.)

Antitoxin for botulism is available and if administered in good time in sufficient dosage, will usually save the patient's life. There are two different strains of *Bacillus botulinus*, and because of this fact it is necessary to make a bacteriologic diagnosis of the offending bacillus in order that the proper antitoxin may be administered. One type of antitoxin will not protect the patient against the other type of bacillus, just as in the serum treatment of pneumonia.

There is a simple household measure which is a guarantee against botulism — namely, the boiling of all canned food. Fortunately the temperature of boiling water destroys botulinus toxin. No canned food which has the slightest odour of rancidity should be used. It is a common error to believe that home-canned foods are safer than commercially canned products with regard to the dangers of botulinus infection. As a matter of fact, all canned goods should be rigorously subjected to inspection and boiling. Experience has shown that in general home-canned foods are the more likely to be insufficiently sterilized.

3. WOUND BACILLI

In time of war the anaerobes always achieve notoriety. They speedily invade tissues which have been injured, as in wounds, and constitute a serious menace to life. There are many anaerobes causing serious infection, and much confusion attaches to their differentiation. They are widely distributed in the soil as well as in the intestinal tract of man and animals.

Anaerobes are usually divided into two principal groups, which may be considered separately. The first is known as the "saccharolytic" group, because its members attack carbohydrates vigorously. To this group belong the disease-producing anaerobic bacilli. The second is known as the "proteolytic" group, because its members attack protein-containing substances vigorously, especially horse serum. The second group of bacilli themselves fail to produce disease, but they are dangerous in the presence of members of the saccharolytic (sugar-dissolving) group. Let us now describe the principal bacilli in the first, or saccharolytic, group.

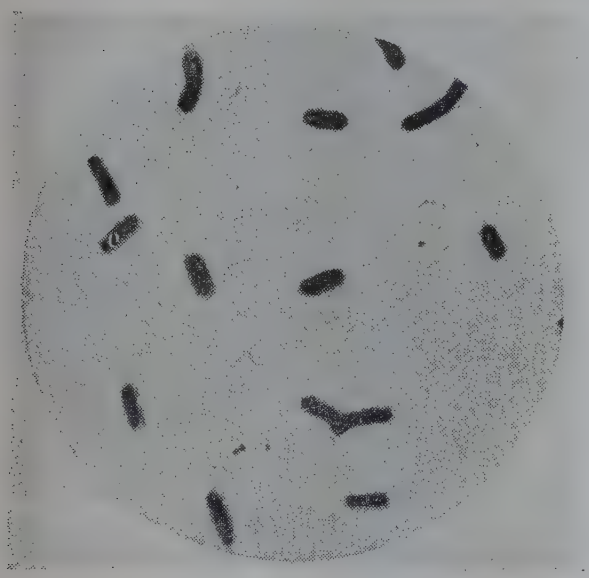


FIGURE 69

The gas-gangrene bacillus, Bacillus welchii (showing capsules). (After Jordan.)

Bacillus welchii, named after Welch, one of the outstanding figures in American bacteriology, was discovered independently by him in the United States in 1892, by Fränkel in Germany a year later, and by Veillon in France in 1897. It is the most important factor in causing gas gangrene, being present in about eighty per cent of such cases. But *Bacillus welchii* does not always cause gangrene. As a matter of fact, surprising though it may appear, it is normally to be found in the intestinal tract of infants and adults. How can this bacillus be at once so dangerous in the blood-stream and tissues generally and remain innocuous in the intestinal tract? The reason for this is that the intestinal tract, in a manner of speaking, really lies outside the body. It is a canal and the mucous membranes which line it are not

ordinarily regarded as permeable to toxins; consequently the mere presence of *Bacillus welchii* in the intestinal tract need arouse no special concern.

Bacillus welchii is a plump, non-motile, Gram-positive bacillus, having a capsule and a large oval spore. (See fig. 69.) It grows best in a medium rich in protein, such as is contained in meat or eggs. It forms acid and gas in most sugars, particularly lactic and butyric acids (the latter having the characteristic disagreeable penetrating odour of rancid butter). The rapidity with which it sours milk, separating the whey or fluid portion from the clot and blowing up the latter with gas bubbles in a "stormy fermentation," distinguishes this bacillus from other anaerobes. (See fig. 70.)

FIGURE 70

Stormy fermentation in milk by Bacillus welchii. (After Jordan.)

Because *Bacillus welchii* attacks the muscle sugar present in tissue with a consequent production of gas, it is known as the "gas or gas-gangrene bacillus." When the abdomen is infected, unusual distention occurs. Delirium, rapid pulse, and high temperature, with a marked discoloration of the diseased tissues, are present in such infections.

Bacillus welchii, like the diphtheria bacillus, excretes a soluble toxin of marked potency. Toxins are horrifying things to conjure with. Just half a drop of *Bacillus welchii* toxin-containing broth, when injected into the muscles of a pigeon weighing three-quarters of a pound, will kill the bird in four to five days.[1] The discovery of toxin leads to the perfection of antitoxin. Just how this is accomplished will be the subject of special consideration later. For the present take note that the Hygienic Laboratory at Washington, D. C., has prepared a *Bacillus welchii* antitoxin so

[1] This is called the "minimum lethal dose" — "M. L. D."

efficacious that one unit will neutralize one thousand minimum lethal doses of toxin. This means that a true *Bacillus welchii* infection can be effectively treated.

The cause of malignant œdema or swelling, *vibrion septique*, is a slender, anaerobic bacillus, also encountered in war wounds. (See fig. 71.) Pasteur first described *vibrion septique* in 1877. It is a Gram-positive, motile, spore-forming rod capable of dissolving red blood corpuscles, and producing a powerful soluble toxin. Antitoxin is prepared in the usual way, by injecting suitable doses of toxin into horses and sheep. *Vibrion septique* attacks

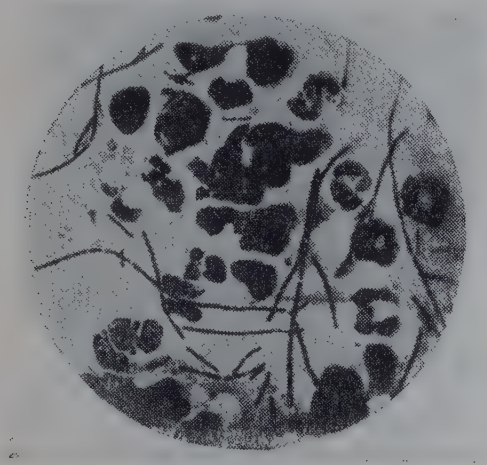


FIGURE 71

Vibrion septique, the cause of malignant œdema (magnified 1000 times). Among blood cells. (After Jordan.)

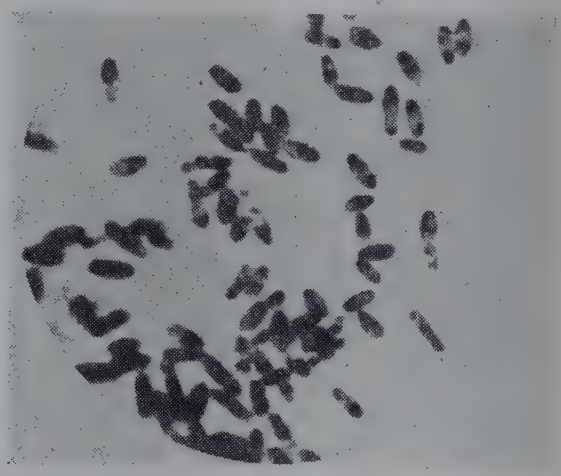


FIGURE 72

Bacillus chauvœi (magnified 1000 times). (After Jordan.)

animals and man, causing blood-poisoning. Infection in man apparently occurs only as a result of wounds. According to Weinberg and Seguin, twelve per cent of wounds examined by them in the World War contained *vibrion septique*.

The cause of blackleg in animals, or symptomatic anthrax, is *Bacillus chauvœi*, which is identical in appearance with *vibrion septique*. (See fig. 72.) *Bacillus chauvœi* does not cause infection in man as does *vibrion septique*, nor has it been found in wounds. It does, however, attack cattle, causing a badly discoloured localized swelling. Hence the name "blackleg." Curiously, it rarely attacks animals less than six months old. And, as a rule, horses, dogs, cats, rabbits, and swine are immune. Cattle may be protected by vaccination, and the United States Bureau of Animal Industry has done much by this means to prevent the spread of blackleg.

Another strict anaerobe, isolated by Weinberg and Seguin in thirty-four per cent of war wounds, is *Bacillus œdematiens*. It is a large, Gram-positive, spore-forming rod. It is less hæmolytic than *vibrion septique* or *Bacillus welchii*. A soluble toxin is produced by *Bacillus œdematiens*, and an antitoxin has been prepared.

Still another anaerobic rod resembling *vibrion septique* is *Bacillus fallax*, found in gas gangrene; but it is of less importance than the other members of the saccharolytic group just described.

This brings us to the second, or proteolytic, group of organisms which are involved in gas gangrene. None of the proteolytic group can produce gas gangrene alone — it is essential that one of the members of the saccharolytic group previously described be present. According to Zinsser, the principal differences between the two groups are that the members of the proteolytic group digest milk without first coagulating it, liquefy and often blacken clotted blood-serum, and usually emit a very offensive odour.

The principal member of the proteolytic group, *Bacillus sporogenes*, in wounds occurs only less frequently than *Bacillus welchii*, Weinberg and Seguin reporting an incidence of twenty-seven per cent. While the disease-producing power of this Gram-positive, motile spore-forming, anaerobic bacillus is practically negligible, it is usually responsible for the putrid odour of wounds. It produces no soluble toxin.

Two bacilli closely resembling *Bacillus sporogenes* are *Bacillus putrificus*, which, like *Bacillus sporogenes*, produces a putrid odour; and *Bacillus histolyticus*, which is not so malodourous.

The anaerobic bacilli of wounds comprise one of the most difficult of all groups in bacteriology. Weinberg and Seguin, Hall, Rettger, M. C. Kahn, and others have done much towards clarification, but accurate differentiation of the members of this group still leaves something to be desired — as no small amount of acrimonious literature on the subject will attest. "In time of peace prepare for war" holds good in the bacteriologic laboratory with more justification than in the arsenal. Gas gangrene caused by anaerobic bacilli is a primary concern in war wounds. With more research in identification of the bacilli and development of

more satisfactory antitoxins or specific drugs, fatalities can be reduced to a minimum.

There comes to mind the heroic deed of Miss K. M. G. Davies recently described by the London correspondent of the *Journal* of the American Medical Association. Miss Davies, the youngest daughter of the lieutenant-governor of the Punjab, was working in 1915 at the American Hospital at Neuilly, Paris, as a bacteriologist under Dr. Taylor of the Imperial Cancer Research. The latter was studying the cause and treatment of gas gangrene. He had obtained satisfactory results in experimenting with guinea-pigs, but could not find human subjects who would permit themselves to be inoculated with the gas-gangrene bacillus. Thus the crucial test was wanting. "Miss Davies, who had studied bacteriology at the Pasteur Institute, had seen 209 fatal cases of gangrene and had seen guinea-pigs die and also recover under Dr. Taylor's experiments. Without revealing her intentions she took a room near the hospital and one day Dr. Taylor received a note from her asking him to come at once and make 'last experiments.' He found that she had given herself two deep injections of the culture of the bacillus in the muscles of the thigh and thus furnished him with a case of pure gas gangrene. He promptly injected the remedy with which he had been working — quinine hydrochloride. She was removed to the American Hospital and in twenty-four hours was pronounced out of danger. By her extraordinary self-sacrifice in taking the risk of a painful and lingering death (for no amputation would have been possible) she proved the efficacy of the treatment and thus saved thousands of lives. The treatment was subsequently used at the American Hospital, but the modesty of Miss Davies prevented any honor from accruing to herself. She desired that the treatment should be preventive and wrote a monograph showing that if the government cloth issued for military uniforms was treated with quinine hydrochloride the infection of gas gangrene might be prevented."

Wounds, particularly war wounds, are the province of the surgeon, but he in turn must rely upon the reports of the bacteriologist. As soon as the offending bacilli have been identified, the appropriate antitoxin is administered. The sewing up of a wound after debridement (excision of damaged tissue) depends

not only upon the kind of bacteria present, but, more important still, upon the number, for there is grave danger of gas gangrene in sewing up a wound which is infected with a large number of anaerobic bacilli such as have been here described. The surgeon waits until the daily report of the bacteriologist shows that the harmful micro-organisms have declined to a negligible number. Only then is it safe to close the wound. Thus through the co-operation of surgery and bacteriology war wounds are robbed of their fatal consequences.

Chapter XIII

INFECTIOUS DISEASES OF ANIMALS

I. PLAGUE

If there were more Pied Pipers of Hamelin, there would be fewer epidemics of plague. Plague is chief among the infectious diseases of animals to which man is likewise susceptible; and rats are the principal agency whereby the disease is transmitted to man. Mice, guinea-pigs, ground-squirrels, and monkeys are also very susceptible to plague, so that it must be considered essentially as an animal disease, to which man also succumbs.

The "Black Death" is no mere figure of speech. From Roman days down to the present time the world has been scourged by epidemics of plague, stigmatized by a frightful mortality rate. It has been estimated that in the fourteenth century one-fourth of the total population, or some twenty-five million persons, perished in the "Great Mortality." After a period of quiescence in western Europe plague flared up in Hong-Kong in 1893 and in India in 1896. Six million persons died in British India, according to official statistics, from 1896 to 1907. In the United States, San Francisco and New Orleans have had their terrifying epidemics. It is not difficult to imagine how demoralizing to industry, commerce, and other phases of daily life plague epidemics can be. Jordan says: "Few diseases have left so deep a mark on general literature. The Decameron of Boccaccio purports to be a collection of stories told by a company of ladies and gentlemen driven by the plague to take refuge in a country house outside the walls of Florence, and one of the most vivid descriptions of the plague ever written is from Boccaccio's pen. Defoe's famous 'Journal of the Plague Year,' although a fictitious narrative, gives a realistic and essentially true picture of the devastation of London in 1665 by an outbreak of the dreaded 'black death,' in which 70,000 persons perished." [1]

Plague attacks people of all ages in all climates, although it is

[1] Jordan: *Bacteriology* (9th edition, 1928), p. 360.

apparently favoured by hot weather. It spreads most rapidly through the slums, filth being an important factor which aids in its transmission. There are two forms of plague in man: bubonic, or glandular, plague; and pneumonic plague. In bubonic plague, so called because of buboes or glandular swellings in the neck, arm-pit, or groin, one encounters headache, backache, apprehension, and dejection. Fever sets in. General blood-poisoning, with hæmorrhages, may follow. In pneumonic plague there is fever, cough, lung congestion, cyanosis (bluish colour of the skin due to insufficient aëration of the blood), and prostration, usually with fatal outcome.

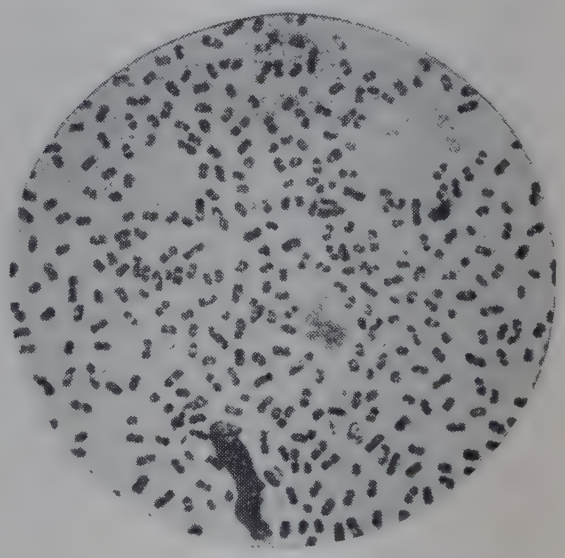


FIGURE 73

Bacillus pestis, the cause of plague. (After Marshall.)

Plague is caused by *Bacillus pestis*, a short, plump rod, staining heavily at the poles. (See fig. 73.) It was discovered independently and simultaneously in 1894 by Kitasato and Yersin. *Bacillus pestis* is non-motile and Gram-negative. It can be readily isolated from the buboes of infected patients and grows well on ordinary media. Unlike most disease-producing microbes, it grows better at 70°F. than at body temperature. When grown in broth overlaid with oil, it forms characteristic long threads like stalactites in grottos. *Bacillus pestis* is favoured in its growth on artificial media by the presence of free oxygen.

Rats, as has already been stated, are responsible for plague in man. More particularly, it is believed that the rat flea carries the infection. It is true, however, that infection in pneumonic plague. especially, may be transmitted from individual to individual by inhaling the infectious droplets expelled in the cough of an infected patient. But this would scarcely account for more than three per cent of the cases in any plague epidemic.

An interesting experiment with rat fleas in a plague investigation in India is often referred to: Two monkeys were placed in separate cages in an animal house in which fleas were abundant. One monkey-cage was protected by fly-paper six inches wide,

for the leap of a rat flea is not more than five inches. The other monkey-cage remained unprotected. At the end of two days five fleas were found caught on the fly-paper surrounding the first monkey. No fleas were discovered upon the animal and it remained healthy. But upon the unprotected monkey two fleas were found and the animal developed a typical case of plague. This clear-cut demonstration of the ability of rat fleas to carry plague has since been amply confirmed.

The prevention of plague therefore depends primarily upon the extinction of rats and defence against fleas. It has been observed that any sudden increase in the mortality of rats generally is an omen that an epidemic of plague is not far behind. Osler points out that three things are necessary to stamp out the disease: "The cleansing of premises, particularly stables and outhouses, so that rats cannot find nesting-places or food; systematic rat-destruction; and making houses rat-proof." Also measures must be taken to prevent the escape or access of rats from ships to the ports at which they stop. Vaccines and serums against plague have been used with varying success.

2. ANTHRAX

Anthrax, which man acquires from insufficiently sterilized brushes, is a particularly fatal disease of cattle and sheep, and goes by the name of "splenic fever." Anthrax attacks horses, swine, goats, guinea-pigs, and rabbits, but rarely domestic animals. Man becomes infected from living animals harbouring the disease or from hides, wool, or bristles which are not thoroughly heated. The bristles of shaving-brushes have achieved particular notoriety in this connexion; consequently no one should use an unsterilized shaving-brush. Anthrax in man has been variously known as "wool-sorter's disease," "rag-picker's disease," and "malignant pustule."

There are four well-defined forms of the disease, two of which involve the skin, the others involving the lungs and intestines respectively. In malignant pustule, which is the first and most common external form of the disease, the symptoms are: itching and the formation of blisters or vesicles, which become the site of inflammation and swelling. The fever rises rapidly and subse-

quently falls even below normal. Death may occur within a few days. In the second external form of the disease, known as "malignant anthrax œdema," the vesicles are absent, but there is more extensive inflammation and swelling, even resulting in a gangrenous condition. This form of the disease is invariably fatal when the inflammation is about the head. The third or pulmonary form of anthrax, known as "wool-sorter's disease," results from the swallowing of infected hair, wool, or dust. There is a sudden chill, with a rapid rise in fever and pains in the chest, back, and legs. The patient is weak to the point of prostration. The mind becomes affected. "There may be vomiting and death may occur within twenty-four hours" (Osler). Similarly, in the fourth or intestinal form of anthrax the infected material — flesh or milk of animals suffering from anthrax — is swallowed. The symptoms resemble those of acute poisoning — chills, vomiting, diarrhœa, fever, pains in the lower part of the body, enlargement of the spleen, and even convulsions.

Of all infectious diseases of animals, anthrax claims the greatest mortality. European herds have been greatly depleted by this disease, which is relatively uncommon in the United States. In Russia, where the disease has been most prevalent, it has been reported that seventy-two thousand horses died of anthrax within one year (1864).

"The discovery of the anthrax bacillus," Zinsser has said, "laid, therefore, as it were, the corner-stone of modern bacteriology." This is so because for the first time in the history of medicine a specific bacillus was shown to be the direct cause of a disease, as demonstrated by Davaine. To be sure, the anthrax bacillus was observed in 1849, by Pollender, who happened to examine the blood of a cow that died from anthrax. But fourteen years later (1863) Davaine suggested that the anthrax bacillus was the specific cause of the disease and furnished experimental evidence by inoculating healthy animals with blood containing anthrax bacilli. The animals promptly came down with the disease. It remained for Koch, however, to supply the general basis for conclusive proof (1876) of the bacteriologic causation of disease, for he introduced the use of artificial media for growing bacilli outside the animal body.

Koch's postulates (see page 54) were established by Davaine

for the anthrax bacillus. Davaine obtained the anthrax bacillus from the blood of infected animals, cultivated them for a number of generations on artificial media, inoculated healthy animals, thereby producing the disease, and finally obtained the identical bacillus in pure culture from the animals which succumbed. Is there any more compelling example of the application of logic to practical ends?

The anthrax bacillus, *Bacillus anthracis*, is a large, nonmotile, encapsulated, Gram-positive rod, with square-cut ends. (See fig. 74.) It is readily grown in the laboratory at all temperatures, forming characteristic skeins of long threads, which under the microscope resemble bamboo rods. Spores are formed during artificial cultivation. *B. anthracis* is the medical student's A B C, because the organism is so large and stains so prettily.

FIGURE 74

Bacillus anthracis, the cause of anthrax, showing spores above. (After Conn and Conn.)

Just how *Bacillus anthracis* produces its fatal effect in man and animals is not altogether certain. It is thought that death is a result of the bacilli mechanically clogging up the very fine blood-vessels (capillaries). Toxins of *Bacillus anthracis* have yet to be found. Pasteur demonstrated that vaccines of this bacillus could be prepared by attenuation — that is, by artificial cultivation at 110°F., which serves to weaken the virulence of the organism. Injection of these heat-weakened bacilli into human beings confers active immunity from anthrax. Passive immunity is obtained by the use of serums.[1]

One of the most common and harmless microbes is *Bacillus subtilis*, the hay bacillus, which, although it is not very closely allied to *Bacillus anthracis*, deserves mention chiefly because of its ubiquity. Essentially a saprophyte, it is frequently encountered as a secondary invader where pus is being formed. It is one of the most obvious of laboratory contaminators, often causing consider-

[1] Another microbe, *Bacillus anthracoides*, resembles *Bacillus anthracis* very closely. It has more rounded ends than the latter and grows more rapidly on artificial media. It is markedly different from the anthrax bacillus, however, in that it does not cause disease. The same is true of *Bacillus radicosus*, another bacillus much like *Bacillus anthracis* in appearance, but somewhat longer and more irregular in shape. A dozen or more other similar organisms have been described, but it is unnecessary for our purposes to enumerate them.

able embarrassment and delay by impairing the purity of cultures. It is a large, Gram-positive, motile rod, growing in long chains and forming spores. The hay bacillus is to be found wherever vegetable matter is undergoing decay, as well as in air and water.

A much smaller rod, *Bacillus astheniæ*, causes a peculiar disease in fowls known as "going light." The bacillus is isolated from the duodenum (just below the stomach) in fowls which show symptoms of starvation and lose weight rapidly as a result of this intestinal infection.

3. GLANDERS

Glanders is an important infectious disease of horses, to which other domestic animals and man are likewise susceptible. Strangely enough, relatively more laboratory workers have succumbed to glanders as a result of accidental infection than have animal-handlers. The acute form of the disease in horses usually involves the nose and lungs and is accompanied by fever and prostration. In the chronic form of glanders, farcy buds occur. These are swellings of the skin and lymph nodes. Curiously, the disease is more fatal to men than to horses. The glanders bacillus, *Bacillus mallei*, is not found in nature except in infected animals or material contaminated by them, such as watering-troughs, mangers, pastures, etc. Consequently, man only contracts the disease by contact with infected animals or their immediate environment.

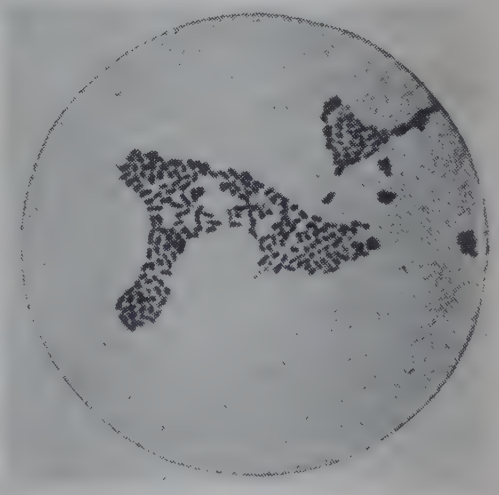


FIGURE 75

Bacillus mallei, the cause of glanders (magnified 1000 times). (After Marshall.)

Bacillus mallei is variable in size, but is usually a small, short, non-motile rod. (See fig. 75.) It stains irregularly, much after the fashion of the diphtheria bacillus, except that it is Gram-negative. The glanders bacillus is aerobic and grows on ordinary media between 72° and 110°F.

An endotoxin (poison within the cell) is formed by *Bacillus mallei*, called "mallein." It differs from most other bacterial

toxins by virtue of its resistance to destruction by heat and storage, but is not a particularly potent poison. Mallein is used as a diagnostic test for glanders, much as tuberculin is used in cattle to establish the presence of tuberculosis, although it is not so satisfactory a criterion as the latter. When mallein is injected into a horse with glanders, it causes a sharp rise in temperature and an intense local swelling. By the use of this test infected animals are identified and healthy stock are safeguarded. Other serologic tests, such as complement fixation and agglutination, are also employed.

At this point it may be well to recall that certain diseases of man find their counterpart in animals. Thus, tuberculosis is caused by different bacilli, known respectively as the bovine (cattle) tubercle, avian (bird) tubercle, and fish tubercle, etc. Johne's disease, a chronic bacterial enteritis of cattle, characterized by intestinal disturbance and inflammation, with a marked loss of flesh, is caused by an acid-fast bacillus resembling the bovine tubercle. A similar disease has been described in sheep. Mention has already been made of rat leprosy, which closely resembles human leprosy.

4. THE BRUCELLA

To Bruce, the great English investigator, who has made major contributions to tropical bacteriology, belongs the distinction of having a group of micro-organisms named after him — the Brucella. Alice Evans, the only woman to have been elected to the presidency of the Society of American Bacteriologists, pointed out the close similarity which exists between Malta fever and the infectious abortion of cattle and almost lost her life in the experimentation. The organism causing Malta fever, first described by Bruce in 1887, is known as "*Bacillus melitensis*." Malta fever is found in all parts of the world, occurring most frequently in and about the Mediterranean. The disease in human beings recalls the symptoms of typhoid fever: malaise, headache, enlarged spleen, and fever lasting two weeks or more. There may be complications involving the kidneys, lungs, joints, etc., and frequent relapses.

Bacillus melitensis is so small a rod that it has frequently been

referred to as a coccus. (See fig. 76.) It is non-motile, does not form spores, and is Gram-negative. It is best cultivated from infected spleens and grows well on artificial media at 100°F. and to a limited extent at temperatures as low as 68°F.

Goats, horses, cattle, and sheep are infected by this bacillus. The high incidence of infection in goats — fifty per cent in Malta and almost that figure in northern Africa — explains how man contracts the disease. Goat's milk is widely used in those regions and it is through goat's milk that man usually becomes infected. Formerly it was believed that one attack of Malta fever was a protection against further attacks, but instances of recurrent infections have been reported.

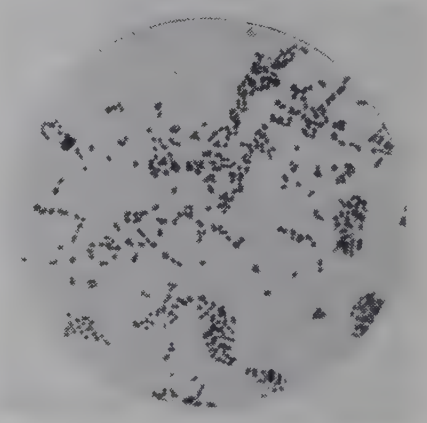


FIGURE 76

The malta-fever bacillus, Bacillus melitensis (magnified 1000 times). (After Jordan.)

As mentioned above, *Bacillus melitensis* resembles very closely the bacillus responsible for infectious abortion in cattle — namely *Bacillus abortus*. In fact, these organisms are indistinguishable by the ordinary cultural methods, and differentiation must depend in the last analysis upon a serologic test (agglutination). Infectious abortion in cattle is analogous to infectious abortion in horses (*Bacillus abortus equi*) and spreads from animal to animal quite as easily. The presence of the offending bacillus in the genital tract of a pregnant animal causes an arrest in the development of the fœtus, or abortion. This is probably due to a poison or toxin contained in the bacillus, which kills the fœtus. The bacillus of infectious abortion may be found not only in the genital tract of infected cattle, but in the milk as well. Strangely, cattle may carry *Bacillus abortus* in their milk without aborting. This offers the possibility of infecting human beings through the same channel as the Malta-fever bacillus. Such infection, however, does not attack the organs of reproduction of women, but either affects the gastro-intestinal tract or causes blood-poisoning.

Bacillus bronchisepticus, a tiny motile rod causing guinea-pig pneumonia is strikingly similar to the bacilli of Malta fever and infectious abortion in cattle.

5. BACILLI OF THE HÆMORRHAGIC SEPTICÆMIA GROUP

The hæmorrhagic septicæmia group of bacilli causes blood-poisoning, hæmorrhages, and intestinal inflammation in many of the lower animals. It is characterized by plump, non-motile bacilli which are Gram-negative. They stain more intensely at the poles. Growth on common media is obtained at ordinary temperatures (77°–105°F.). Free oxygen appears to be preferred by this group of organisms. Gelatin is not liquefied by them. The most important representatives of the hæmorrhagic septicæmia group are the bacillus of chicken cholera and the bacillus of swine-plague.

The bacillus of chicken cholera, *Bacillus avisepticus*, causes an acute infection in fowl, especially in chickens, ducks, and geese. The result is diarrhœa, exhaustion, inflammation, and blood-poisoning, usually terminating fatally within a few days. Pasteur's research with this organism is of more than passing interest. Not only was he the first bacteriologist to describe *Bacillus avisepticus*, but with it he made the first attempt at vaccination by means of attenuated cultures injected in small doses. (This subject of vaccine therapy will be treated more fully in a later chapter.) Moreover, with *Bacillus avisepticus* Pasteur showed for the first time that it was possible to separate toxin from bacteria by filtration through a fine unglazed porcelain filter which permits the toxin to pass through its pores, but prevents the passage of bacteria.

The bacillus of swine-plague, *Bacillus suisepticus*, is practically identical with the bacillus of chicken cholera. It is responsible for epidemic pneumonia in hogs, which is followed by blood-poisoning. The intestinal tract, however, remains unaffected, as contrasted with infection by the hog-cholera bacillus (*Bacillus suipestifer*), which is localized in the intestinal canal.

6. TULARÆMIA

California ground-squirrels, rabbits, and wild game are subject to infection by *Bacillus tularense*, a very small rod, causing a disease somewhat similar to plague. The organism was first described by McCoy in 1911. Recently Francis described cases in

which it has been shown that man may become infected by the same bacillus, probably transmitted by the deer fly and the wood tick. The disease, known as tularæmia, occurs in two forms: as an inflammation of the glands; and as an irregular typhoid-fever-like condition. Men engaged in handling and dressing infected market rabbits have contracted the disease. Fortunately, it is rarely fatal.

The diseases enumerated in this chapter by no means comprise all the infectious diseases of animals, but they are sufficiently representative to establish two points: first, that bacteria are versatile in choosing their hosts; and, secondly, that man is not only the victim of infectious diseases peculiar to his own constitution, but must suffer the diseases of his antecedents, evolutionally speaking, as well. Animals, however, do not suffer from strictly human diseases. The problem of controlling human infectious disease is difficult enough without the further complication of eradicating animal disease. The vivisectionists are likely to forget the service that bacteriology, regardless of the motive, has rendered our animal friends by protecting them from fatal epidemics. Theobald Smith tells of an unusually enlightened officer of the Society for the Prevention of Cruelty to Animals in Washington, D. C., who urged him to prosecute his experiments on guinea-pigs in order to save the horses of that city from glanders. In protecting animals from infectious disease we protect ourselves.

Chapter XIV

CHOLERA

Cholera, like typhoid fever, is spread chiefly through the agency of infected water. In their intensity and appalling mortality Asiatic cholera epidemics have rivalled plague. Five great epidemics of cholera occurred during the nineteenth century alone. A bathing festival on the Ganges in India in 1891 initiated a world-wide epidemic. It claimed many victims among the pilgrims and was carried by them westward into Germany, where it broke out with violence in Hamburg. From that port it followed ocean traffic to America and Africa. According to Zinsser, "during this epidemic in Russia alone eight hundred thousand people fell victims to the disease."

There are three important stages in cholera. First, there is a mild diarrhœa. Secondly, an intense diarrhœa develops, the stools becoming pale, watery, and opalescent, often called "rice-water stools" because they resembled the water which is drawn off after rice has been cooked. In this stage of the disease vomiting and cramps are frequent. There is usually cyanosis (blueness of the skin). The patient may go into a coma. Finally, the third stage — if the patient survives — is one of reaction, with a consequent alleviation of symptoms. Always there is grave danger of complications which resemble those of typhoid fever. Pneumonia, pleurisy, and inflammation of the mucous membranes of the throat and genitals are not uncommon sequelæ of cholera.

Asiatic cholera is caused by the vibrio or spirillum of cholera. Koch, the creator of the science of infectious diseases, discovered the cholera spirillum in the stools of cholera patients (1883). It is a short, slightly curved or twisted rod, which gives it the synonym of "comma bacillus." Short spirals or S-shaped forms are also of frequent occurrence. Active motility is due to a single polar flagellum. The microbe is Gram-negative. Ordinary and special alkaline artificial media are used to grow the

organism from the stools of infected patients or other suspected materials. The cholera spirillum multiplies readily at a temperature from 65°F. to 100°F. It prefers the presence of free oxygen. (See fig. 77.)

The progress of bacteriology as a science is marked by the tombstones of many martyrs. Dr. Emil Oergel, an assistant in the Hamburg Hygienic Institute, became infected with the cholera spirillum by accidentally sucking up into his mouth some fluid from an infected guinea-pig with which he was experimenting. He developed a typical case of cholera, although there was no cholera in the city at the time. A nearly pure culture of the organism was found in his stools and he died within nine days. Two other German investigators, Emmerich and Pettenkofer, in order to prove the validity of Koch's contention that cholera was caused by his microbe, voluntarily partook of a small amount of a broth culture of "Koch's vibrio." Emmerich became seriously ill with genuine Asiatic cholera, which almost proved fatal. Pettenkofer got off with a diarrhœa.

FIGURE 77

Spirilla of Asiatic cholera (magnified 1000 times). (After Jordan.)

Not all individuals are equally susceptible to the disease. Jordan states that "the reason for this probably lies partly in individual differences in natural innate resistance, partly in the fluctuations that occur in such resistance. It is well known that when cholera is prevalent, certain persons contract the disease and succumb to it more readily than others apparently equally exposed to infection. Fatigue, the excessive use of alcohol, and various factors leading to mild, non-specific gastro-intestinal derangements, predispose in a marked degree to attacks of cholera." Animals do not spontaneously contract the disease although they can be artificially inoculated.

As with typhoid fever, there are cholera carriers who harbour the microbe in their intestinal tracts and are able therefore to infect other individuals. This means that despite quarantine inspection the disease may be brought in from across the seas.

Four such cases occurred in the United States in the summer of 1911. An employee who had previously been guarding apparently healthy immigrants at quarantine suddenly developed the disease a week later. Obviously, one of his charges harboured the cholera organism without the fact becoming known.

Cholera, as has been mentioned, is spread chiefly through contaminated water-supplies used for drinking, cooking, and washing. A perfect example was the Hamburg epidemic. The Elbe was contaminated by sewage, and from this unfiltered river water, infection took place. Milk as well as water may be contaminated; likewise uncooked vegetables which have been washed in polluted water. Flies, always to be feared as carriers of microbes, readily infect food-supplies, for the cholera organism may live in their intestines for several days.

The isolation of infected individuals is a prime necessity in preventing the spread of cholera. Cleanliness, disinfection of excreta, etc., are also important prophylactic measures. In treatment dietary restrictions, too, are of value. Favourable results have been reported in cholera patients following injections of salt water of the proper concentration.

There is considerable question as to whether or not the cholera spirillum produces a true soluble toxin.[1] It is of interest that a single attack of cholera protects against subsequent infection. Vaccination against the disease by means of killed or attenuated cultures of the microbe has proved fairly successful and is analogous to vaccination against typhoid fever. Haffkine,

[1] There are a great number of cholera-like spirilla which are difficult to differentiate from the true cholera spirillum, such as *Spirillum metchnikovii*, discovered by Gamaleia in the intestinal tract and blood of fowls suffering from a disease closely resembling fowl cholera. It differs from the true cholera spirillum in that the latter does not infect pigeons, whereas the former causes fatal blood-poisoning following injection of relatively few organisms. There are several other spirilla which do not produce disease in man, among them being:

Spirillum massaua, isolated from human stools, which resembles *S. metchnikovii* more closely than it does *S. choleræ*.

Spirillum of Finkler-Prior which resembles *S. choleræ* except that it is somewhat larger, not so regularly curved, does not give the typical cholera-red reaction, and fails to fulfil the serologic tests.

Spirillum deneke, isolated from butter, which closely resembles spirillum of Finkler-Prior.

Spirillum phosphorescens, isolated from river water in Germany, which yields luminous cultures and is also closely allied to the spirillum of Finkler-Prior.

particularly, has reported excellent results on a large number of individuals in India. Recent army experience confirms the observation that vaccination against cholera materially reduces the incidence and mortality from this dread disease. Thus, in the Greek Army during the Balkan War twenty per cent of deaths from cholera occurred among soldiers not vaccinated; three per cent in soldiers vaccinated once; and only one per cent in soldiers vaccinated twice. Zinsser says: "Vaccination must be repeated certainly every two years and probably more often in the case of armies in the field."

Chapter XV

SYPHILIS

Syphilis is an infectious disease of profound individual and social significance, and its history is of more than passing interest. It has been said that the disease was known to Asiatic antiquity. There is considerable doubt as to when syphilis first made its appearance, but until recently the consensus of opinion was that Columbus discovered more than America on his first voyage to Haiti. In any event the inhabitants of Barcelona became infected with syphilis soon after Columbus returned. Thence the disease spread to Italy in 1493. It was introduced by the invading army of Charles VIII, to which were attracted Spanish mercenaries, many of whom had contracted the disease. Osler says: "His soldiers syphilized Naples; the disease spread throughout Italy, and in a few years Europe was aflame." The name "syphilis" appears first in 1530 in a poem by Fracastoro, "Syphilus" being the name of the infected hero. Take note that at this stage in medical history syphilis took on the character of an epidemic and the disease was of great severity. "Civilization is syphilization" — Krafft-Ebing's memorable aphorism — gives point to man's acclimatization to this infection. At the present time syphilis is no longer considered a fatal epidemic disease, for man has become better adapted to it. Accurate statistics concerning its incidence are still wanting, but in general it is believed that five to ten per cent of the general population have been infected at some time or other with syphilis.

Of all diseases syphilis is the most loathsome and vicious; yet it begins inauspiciously enough as a small lesion called a "chancre." Commencing as a small red papule, a chancre gradually enlarges to the size of a pea or even a cherry. Then it begins to ulcerate. The edges become hard, or indurated. The ulcer then begins to granulate and may heal with or without treatment, leaving only a very slight scar or often no scar at all. The most prevalent site for the initial lesion of syphilis is, of course, in the genitals.

It is generally assumed that syphilis is altogether a venereal disease resulting directly from sexual intercourse with infected individuals. To be sure, this is the most common mode of transmission. Chancres may also occur on the fingers, lips, and nipples as a result of sexual perversions with syphilitics. But there are numerous instances on record of accidental infection through non-venereal channels. Members of the medical profession, nurses as well as doctors, have frequently become innocent victims. Another important mode of infection of this disease is congenital transmission, often erroneously termed "hereditary" transmission. As has been stated before, no infectious disease is transmitted hereditarily — the child is infected either in the womb or while being delivered. It is noteworthy that a woman who has borne a syphilitic child is herself immune and cannot be infected by the child. (This is known as "Colles's law.") However, there is no question but that syphilitic parents bring syphilitic offspring into the world.

Syphilis is a protean disease. Its four principal stages may be characterized as follows: *Primary stage.* Within a month from the time of exposure of infection a small ulcer or chancre develops, the walls of which usually become hard or indurated. During the six to twelve weeks following the original infection, no other particular impairment of health is noted. *Secondary stage.* The principal feature of these "secondaries," which develop five or six weeks after the chancre, is a slight rash of coppery tint which does not itch and disappears without treatment, and is therefore often overlooked. Other manifestations are sore throat with small grey ulcers in the tonsils and, still more important, flat grey areas on the mucous membranes of the mouth and throat, called "mucous patches." The hair loses its gloss and may fall out; the lymph glands become enlarged; the joints may ache and the eyes become congested. Fever and anæmia (insufficient red blood cells) occasionally follow. This secondary stage may last about two years, but has no definite time limit. *Tertiary stage.* All the tertiary manifestations may be reduced to one common denominator, a chronic inflammation of the cellular tissue, an inflammation which may either be diffuse, as in the liver, or localized, as in a so-called gumma. This gumma is a firm painless swelling which develops

rapidly, enlarges, softens, ruptures, and discharges its contents, thus resulting in an ulcer. No tissue or organ of the body is exempt, a gumma may develop anywhere. When fully developed, it is a circular ulcer, with steep walls and "punched out" floor, with an infiltrated base. When located in bones or important internal organs, it may lead to terrible destruction, with either permanent disfiguration or impairment of vital function.

In a small percentage of syphilitic patients a fourth stage occurs. *Quaternary stage — tabes dorsalis* (or locomotor ataxia) and general paralysis, or softening of the brain, causing insanity. The former is a rather chronic condition due to the presence of the syphilitic germ in the spinal cord, whereas general paralysis or paresis is a well-defined mental disease, which, if not properly treated, leads to a rather pitiful end within a short space of time.

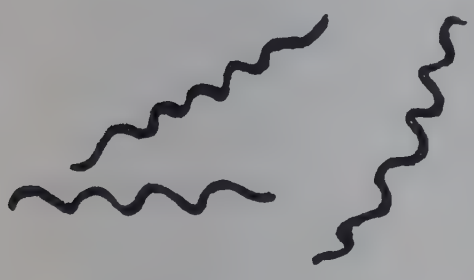


FIGURE 78

The cause of syphilis, Spirochæta pallida. (After Conn and Conn.)

"With the exception of the primary sore, every feature of the acquired disease may be seen in the congenital form" (Osler). It seems heinous that children should be brought into the world with such afflictions of the skin, eye, ear, nose, and teeth as to handicap them beyond measure. Such children rarely thrive; growth is slow and development tardy. They are indelibly and shamefully stigmatized. But much can be done by modern medicine to ameliorate their condition.

Syphilis has ravaged the world since 1493, but it was not until more than four hundred years later, in 1905, that the cause of the disease was established. Schaudinn and Hoffman discovered in syphilitic tissues the characteristic extremely delicate, undulating spiral microbe called "*Spirochæta pallida*" or "*Treponema pallidum*." It is distinctly motile in fresh preparations, as may be readily seen upon microscopic dark-field illumination. (See fig. 78.) The undulating spirals stand out like rows of throbbing electric lights against a black sky. The movement of *Spirochæta pallida* is well described by Zinsser as "a rotation about the long axis, gliding movements backward and forward, and, occasionally, a bending of the whole body. Its con-

volutions, as counted by Schaudinn vary from three to twelve . . . forming acute, rather than obtuse, angles. The ends of the micro-organism are delicately tapering and come to a point." The organism stains with such difficulty that special methods are required for its demonstration in fluids and tissues. *Spirochæta pallida* is the cause of paresis.

It is extremely difficult to cultivate spirochætes in the laboratory. Noguchi finally succeeded in developing a satisfactory method, based on the use of a small piece of sterile kidney-tissue taken from a rabbit. The small piece of kidney is placed at the bottom of a long test-tube containing human ascitic fluid (obtained from the abdomens of patients with dropsy) and overlaid with mineral oil to exclude free oxygen. In such a medium the spirochætes form a cloudy zone of growth. After prolonged cultivation on artificial media, however, the spirochæte loses its virulence. *Spirochæta pallida* is found primarily in the initial lesion, the chancre; in the mucous patches present in the secondary stage of the disease; in the brain and spinal cord in cases of neurosyphilis; but only very rarely in gummas or skin eruptions.

The diagnosis of syphilis depends chiefly upon a thorough physical examination with particular attention to marked skin changes. The laboratory is always of considerable aid in diagnosis on furnishing reports on the Wassermann reaction or Kahn test on blood or spinal fluid. The Wassermann and other tests are generally regarded as satisfactory criteria of syphilitic infection, yet for the most part they involve a laborious technic, which varies in the hands of different workers, resulting at times in contradictory findings. Thus, one private laboratory may report "one plus" (+) while another laboratory will report "negative" (−) on the same blood specimen. State laboratories and those belonging to the better hospitals are so well standardized that such contradictory results are relatively infrequent. A doubtful result should, of course, always be duplicated. In the final analysis, the Wassermann test alone is an insufficient basis for a positive diagnosis — the clinical findings should always receive prior consideration. Innumerable modifications and substitutes for the Wassermann test have been devised; each laboratory technician becomes a law unto himself, and each

syphilologist a court of appeal. In syphilis which involves the brain and spinal cord other accessory procedures, such as the colloidal gold or benzoin tests are also of value.

Syphilis is a preventable disease. It follows, therefore, that general paralysis, which is an advanced stage of syphilis, would never occur if syphilis were not permitted to develop. Irregular intercourse will probably persist as long as there are desirous men and willing women — or vice versa — but there are two measures which can be employed to safeguard the individual and society against syphilis. The first is personal hygiene, which includes continence, or, failing that, immediate prophylaxis after exposure. The proper use of "blue" (mercury) ointment before and directly after intercourse is effective in preventing infection. Recent army experience demonstrated this beyond question. The second measure is administrative; it includes inspection, segregation, and compulsory registration of venereal disease.

Society would do better to educate its members in personal hygiene than to enforce regulations which are easily evaded. The medical profession aims to subject every prospective bridegroom and bride to a complete blood examination before the marriage certificate is issued. As yet, most legislators have been reluctant to embody this in their statutes, although such a law would prove more beneficial to mankind than any number of "blue" laws. For, if syphilis is discovered early — that is, even before obvious symptoms appear — treatment will be effective in the prevention of later unhappy manifestations of the disease. One can only deplore the traditional attitude of secrecy concerning venereal disease. Perhaps the time is not far off when every individual will have sufficient knowledge to prevent infection from *Spirochæta pallida.*

Contrary to popular belief, syphilis is not only preventable, but amenable to treatment, particularly in the early stages. There are few chapters in science more stimulating than the reports of Ehrlich's painstaking search for the perfect remedy. It will be remembered that six hundred and five compounds for the treatment of syphilis had been tried by him and found wanting before he discovered arsphenamine, better known by the trade name of "salvarsan." Consequently it is known as

"606." Neo-arsphenamine or neosalvarsan, "914," is a still further improvement, and represents three hundred and eight more painstaking trials. Both "606" and "914" depend on their content of arsenic to check the spirochætes. Mercury and iodides should also be used in treatment. The theory underlying the use of arsenic-bearing drugs or any others in syphilis is to introduce enough poison to kill the spirochætes, but not enough to damage the surrounding tissues. Ehrlich found that *Spirochæta pallida* was especially susceptible to arsenic; hence the latter is called a "specific." Obviously, the quacks prescribing nostrums to be taken internally and guaranteeing cure, or those purporting to possess some secret preparations, some "*therapia sterilisans magna*," simply bamboozle a timorous and ignorant public. The site most commonly used for the injection of arsenicals is some prominent vein in the arm, although spinal, muscular, and subcutaneous injections are likewise employed.

Antisyphilitic treatment must be instituted early and carried through rigorously. Procrastination means further development of the disease, making the infected agent more dangerous to society. Osler says: "That the later stages which come under the charge of the physician are so common, results, in great part, from the carelessness of the patient, who, wearied with treatment, cannot understand why he should continue to take medicine after all the symptoms have disappeared; but, in part, the profession also is to blame for not insisting more urgently that acquired syphilis is not cured in a few months, but takes at least three years, during which time the patient should be under careful supervision." The family physician is often called upon for advice concerning syphilis and marriage. Providing that the patient has been entirely free of symptoms for one year, at least two full years should elapse between the date of infection and marriage.

General paralysis develops in about five per cent of persons who have contracted syphilis. It occurs chiefly between the ages of forty and fifty. Males are affected much more frequently than females. It has been suggested that pregnancy so modifies the reaction to syphilitic infection as to account for this difference between the sexes. Yet, as might be expected, the incidence of general paralysis is much higher in married than in single

persons. It is noteworthy that this form of insanity occurs more frequently in urban than in rural communities. Alcohol and other excesses in syphilized individuals are contributing factors to general paralysis. To quote Osler: "The habits of life so frequently seen in active business men in our large cities and well expressed by the phrase 'burning the candle at both ends' strongly predispose to disease." According to the best evidence obtainable, general paralysis is only about two hundred years old. Statistics from New York State, evaluated by Kirby, show that a high point was reached in 1918 and that there has been a subsequent decline, due to more education, prophylaxis, and improved methods of treatment. Curiously enough, as syphilis loses its severe epidemic qualities in the course of centuries, general paralysis becomes more frequent. Some authorities now claim that the latter is also gradually changing its character to a milder, longer course.

While arsphenamine (salvarsan) and neo-arsphenamine (neosalvarsan) are effective in syphilis, their value in the treatment of general paralysis has been considered slight or even non-existent. But now the situation has been greatly brightened by the introduction of malarial therapy. Wagner von Jauregg received the 1927 Nobel prize for this brilliant contribution to medical science. In brief, malarial therapy is carried out as follows: The general paralytic is inoculated with blood from a malaria patient. Within a week he develops a typical benign tertian malaria, which generally means a rise in temperature every forty-eight hours, followed by a chill. After about ten chills the malaria is checked by quinine. The paralytic then gains weight rapidly and in about one-third to one-half of the cases improves remarkably. Whereas the paralytic previously spoke grandiloquently of his trillions of dollars and thousands of wives, with slurring speech and tremor of the tongue, after treatment he returns to normalcy and can resume his place in the home, in business, and in society. Tryparsamide, an arsenical prepared at the Rockefeller Institute for Medical Research by Jacobs and Heidelberger, has also yielded good results in the treatment of general paralysis.

The New York State Psychiatric Institute and Hospital has done much research on the treatment of general paralysis, and

the papers published by Kirby and Bunker are largely responsible for establishing malarial therapy on a sound basis in the United States. It is heartening to know that general paralysis can be swerved from its tragic course. The disease does not occur except when it follows syphilitic infection. In a sense, therefore, social enlightenment may be looked upon as the best means of wiping general paralysis out of existence.

Chapter XVI

OTHER SPIROCHÆTAL DISEASES

I. RELAPSING FEVER

Spirochætes and syphilis having become almost synonymous terms, one is likely to overlook the fact that there are still other spirochætal diseases of importance. Chief among these is relapsing fever, also known as "recurring" or "seven-day" fever. It is prevalent in India, Africa, and other tropical countries. Epidemics have occurred in the southern part of the United States and in Europe, particularly in Russia. As the name implies, the disease is characterized by a sporadic rise in temperature. The onset is usually abrupt, starting with a chill, rapid rise in temperature, and severe pain in the back and limbs. Delirium is not uncommon where the fever is high. The spleen becomes enlarged and jaundice may set in. The fever lasts from three to ten days and then a crisis occurs. Following this the temperature drops rapidly, as in pneumonia, and the other symptoms disappear as suddenly as they formerly appeared. In about two weeks there is usually a recurrence of symptoms, as a rule of lesser intensity and shorter duration than the original attack. Several relapses may ensue throughout a lifetime, the disease seldom being fatal.

Recurring or relapsing fever is caused by a spirochæte which was discovered by Obermeier in 1873. It resembles the *Spirochæta pallida* very closely, for it is a delicate, actively undulating filament. Noguchi has cultivated it artificially in the same fashion as *Spirochæta pallida*. Other methods have also been used with success. Monkeys, rats, and mice may be inoculated with the disease, but dogs, rabbits, and guinea-pigs are apparently immune. Carlisle has described the case of an investigator who was accidentally bitten by a monkey which had been infected for experimental purposes. The victim had a paroxysm, fever, severe frontal headache, and sharp pains in the back. There was

a rapid decline in temperature and apparently complete recovery. In about a week there was a second paroxysm, and finally a third, yielding a typical picture of relapsing fever.

There are several distinct types of spirochætes responsible for relapsing fever in different localities. The organism described above is called "*Spirochæta recurrentis*" or "*obermeieri*," after its discoverer. There is some question whether this organism is the one responsible for the African form of the disease, which was formerly considered to be a kind of malaria. Koch contended that the East African spirochæte was smaller in size and caused milder symptoms in man and more severe symptoms in animals. This organism is known as *Spirochæta kochi*.

Another closely allied strain is *Spirochæta duttoni*, a larger spirochæte than *obermeieri*, causing West African tick fever. Dutton and Todd showed that the disease was transmitted by the bite of a tick. The tick becomes infected by sucking blood from an infected human being. Not only can the tick then infect other individuals, but the eggs of the female tick are also infected and therefore hatch out into infective ticks. While no such intermediate host has been discovered for *Spirochæta obermeieri*, "it is known, however, that the organism can live in the bodies of bedbugs and it has also been suggested that lice may be the carriers" (Zinsser). The latter are believed to transmit North African relapsing fever, which is caused by *Spiroschaudinnia berberi*. Relapsing-fever spirochætes are not restricted to tropical climates, for certain forms have been found in the United States: *Spirochæta novyi*, etc.

One siege of relapsing fever, like smallpox, usually renders the patient immune from subsequent infection with the same organism. It has been shown that the blood of man and animals recovering from relapsing fever possesses specific substances which destroy the spirochætes. The serum from these animals, therefore, when injected into other animals, confers a passive immunity. The treatment of relapsing fever by arsenicals, unlike syphilis, has not yielded such satisfactory results. It is interesting to note that general paralytics have been artificially inoculated with relapsing fever on the same principle as that of artificial malaria and that the results of these two methods compare favourably. The chief obstacle to the use of relapsing fever in

such cases is that it is not so easily controlled and checked as is malaria by quinine.

Before leaving the disease-producing spirochætes which resemble *Spirochæta pallida* very closely, mention may be made of two new species isolated by Noguchi from ulcers on the human external genitalia and from wart-like growths. These are called respectively: "*Spirochæta phagedenis*" and "*Spirochæta calligyrum.*"

2. MOUTH SPIROCHÆTES

"Trench mouth," better known as "Vincent's angina," is an inflammation which is characterized by white, painful patches of the mouth, tonsils, and throat. In its inception the disease resembles diphtheria because of the formation of a pseudo-membrane; later it resembles syphilis, because of severe punched-out ulcerations. It is most uncomfortable at all times. Because the disease is caused by organisms found in the soil, many cases were observed among the soldiers in the trenches during the World War. Local epidemics are not infrequent.

A variety of bacilli and spirilla is always to be encountered in the mouth under such conditions and it is still an open question which organism is responsible for the disease. The spirilla usually present differ from *Spirochæta pallida* in that they have flatter and less uniform undulations as compared with the acute angles of the latter. Invariably there have also been found long, pointed, non-motile, fusiform bacilli (*Bacillus fusiformis*) associated with the spirilla. Vincent, Plaut, and others have demonstrated their constant presence in Vincent's angina. They form characteristic thread-like colonies when grown on a solid medium. In staining, *Bacillus fusiformis* is usually Gram-negative and more sharply stained at the poles.

The disease can be readily treated by the use of neo-arsphenamine (neosalvarsan) locally or by injection into the veins. Sodium perborate solution as a mouth wash has also yielded excellent results. Dentists are sometimes puzzled by this disease if they have not had previous experience with it, but they have no difficulty in obtaining gratifying results by use of the treatment just mentioned when the diagnosis is established.

Fusiform bacilli, which can scarcely be differentiated from

those of Vincent's angina, are frequently encountered in decayed teeth, unclean gums, etc. They have been found together with spirilla in noma, a gangrenous disease of the gums and cheeks.

Not all spirochætes in the mouth produce disease. Many are harmless and normal inhabitants.[1]

3. YAWS

Yaws, or "*frambœsia tropica*," is a tropical disease almost identical with syphilis in its symptoms and particularly in the microbe which causes it — *Spirochæta pertenue*. This organism was discovered by Castellani in 1905. It is a long, slender undulating filament, with as many as twelve spirals. Zinsser states that: "Studies on yaws have satisfactorily proven that yaws is not transmitted in the same way as lues [syphilis], probably passing from individual to individual by casual contact. Whether or not insects are involved is still uncertain. It yields readily to arsphenamine [salvarsan], more readily than lues, and complete cure seems to be more easily attained than in the other disease."

4. ANIMAL SPIROCHÆTES

Man is not alone in playing host to the spirochæte. Chickens, particularly in South America, suffer from an acute infectious disease caused by a spirochæte which closely resembles the spirochæte of relapsing fever. The disease is characterized by an abrupt onset, fever, diarrhœa, exhaustion, and high mortality. The causal microbe has been appropriately named "*Spirochæta gallinarum*." It attacks other fowl, such as ducks, geese, and pigeons, but does not infect mammals. *Spirochæta gallinarum*, like the relapsing-fever spirochæte, depends upon the tick as an intermediate host.

[1] *Spirochæta buccalis* is about twice as long as *Sp. pallida* and has from three to ten irregular flat coils.

Spirochæta dentium is very similar in size and general appearance to *Sp. pallida*.

Spirochæta macrodentium is midway in size between the two above-named organisms. Its spirals are less regular than those of *Sp. pallida*, and it stains more intensely.

Spirochæta refringens, slightly longer and thicker than *Sp. pallida*, is frequently found associated with the latter in syphilitic tissues. It has fewer and flatter undulations, is more active, stains more deeply, and is highly refractive when living.

There is a spirochætal disease of geese, so closely resembling that just described for chickens as to be indistinguishable. This disease, which has been studied in Russia and northern Africa, was found by Sacharoff to be caused by *Spirochæta anserina.*

Rats carry not only plague, but also the spirochæte which causes rat-bite fever or "sodoku." This disease in man is characterized by high fever, local inflammation, enlarged lymph glands, and unsightly and painful skin eruptions. As in relapsing fever, the febrile temperature subsides for several days and then recurs. Futaki and his Japanese co-workers discovered that this disease was caused by *Spirochæta morsus muris.* Recently Solomon reported favourable results in general paralytics following inoculation with this disease, on the same basis as that of malaria and relapsing-fever therapy.

House and field rats carry another spirochætal disease, known as "infectious jaundice" or "Weil's disease," which has been epidemic in many localities. It is characterized by gastro-intestinal symptoms, fever, jaundice (yellowing of the skin) and enlargement of the liver and spleen. The disease is rarely fatal in the United States, but it has claimed victims in Alexandria and other cities.

The cause of this disease has baffled many investigators, each indicting one bacillus or another. But in 1916 Inada and his Japanese colleagues established that *Spirochæta icterohæmorrhagiæ* was responsible for infectious jaundice. It may be mentioned parenthetically that Noguchi classes this organism with the leptospira, the most important of which will be discussed in the next chapter. *Spirochæta icterohæmorrhagiæ* is thicker and more irregular than *Spirochæta pallida* and more easily cultivated. It has no terminal flagella.

Blood from convalescent patients or especially prepared serum has proved effective in the treatment of infectious jaundice. Prevention of the disease depends upon the extermination of rats, the safeguarding of food and soil against contamination, and the segregation of infected patients.

Even the oyster has his special spirochæte. *Spirochæta balanitidis* is a slightly shorter and thicker spirochæte than *Spirochæta pallida.*

And there are others too numerous to mention.

Chapter XVII

YELLOW FEVER

The story of yellow fever reads like sheer romance. Here is a disease, never absent from the ports of tropical South America or Cuba, which has swept in epidemics over the tropical Atlantic into the United States and has come as far north as Philadelphia, leaving a frightful mortality in its wake. Eighty out of every hundred patients have died during severe epidemics.

"Yellow Jack," or "black vomit," is the name by which this scourge is known. A yellowing, flushed face, rapidly rising temperature, slowing pulse, vomiting of blood, excessive excretion of albumin, and often delirium are its symptoms. Like syphilis it is a disease confined to human beings.

Many theories have been advanced as to the mode of transmission of yellow fever, but it was not until Finlay suggested the mosquito as an intermediate host that scientific researchers were put upon the right track. (See fig. 79.) The brilliant work done by Reed, Carroll, Agramonte, and Lazear, all Americans, and Noguchi, is now a familiar history of martyrdom to science. (See figs. 80, 81, 82, 83.) After nine unsuccessful experiments Carroll allowed himself to be bitten by an infected mosquito. Four days later he came down with a severe attack of yellow fever, which threatened his life at the time and subsequently was responsible for his death. Soon after Carroll's experience Lazear, while examining yellow-fever patients in the hospital, observed that a mosquito had alighted upon his hand. He could kill it and play safe, or he could let it bite him and corroborate Carroll. He deliberately permitted the mosquito to gorge itself with his blood. In five days he was in the grip of a vicious attack of yellow fever. He paid for this crucial experiment with his life.

Other volunteers contracted yellow fever during further experiments, which established beyond doubt that mosquitos could transmit yellow fever. But the question still remained:

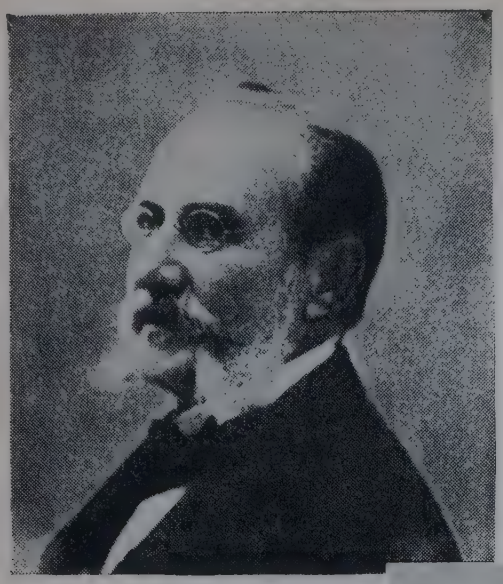


FIGURE 79
Finlay.
(After Kelly.)

FIGURE 80
Walter Reed.
(After Kelly.)

FIGURE 81
Carroll.
(After Kelly.)

FIGURE 82
Agramonte. *(After Kelly.)*

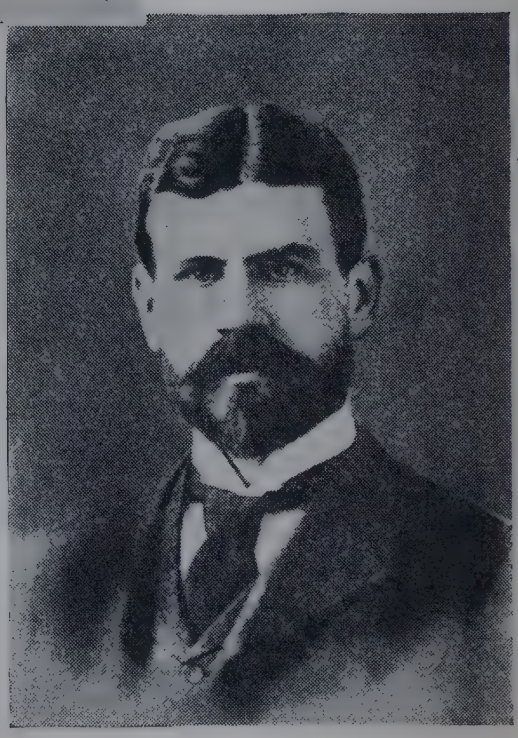


FIGURE 83
Lazear. *(After Kelly.)*

Were mosquitos alone responsible for the transmission of yellow fever or were there other agents, such as excreta and vomitus, capable of transmitting this disease? This important query led to a spectacular experiment. Three volunteers consented to inhabit an especially built mosquito-proof house under the most revolting conditions. The house was heated artificially to 90°F. and the air made still more humid by the vaporization of water. It was more tropical inside the house than out, even though the scene was laid in Cuba. But the heat and the humidity were the least unpleasant features. Spanish inquisitors could scarcely have devised such details of filth.

FIGURE 84

Camp Lazear. (*After Kelly.*)

Everything with which they came in contact, wearing-apparel, household dishes, bedding, etc., were smeared with vomitus, fæces, and blood of yellow-fever patients. "Each evening, before going to bed, they unpacked and thoroughly shook clothing and bedding of yellow-fever patients, and hung and scattered these materials about their beds. They slept, moreover, in contact with linen and blankets soiled by patients" (Zinsser). This was the daily routine for twenty consecutive nights. Their only consolation was that no mosquitos could bite them. (See fig. 84.)

The experiment was successful — not one of the three men contracted yellow fever. Subsequently the experiment was twice repeated with the same negative outcome. In order to set the final seal on the proof that mosquitos alone were responsible

for the transmission of yellow fever, four of the volunteers then allowed themselves to be bitten by infected mosquitos and contracted yellow fever. But it is not any mosquito that can act as an agent, — it is a very particular kind of mosquito, *Stegomyia fasciata*, — and then only the female of the species. *Cherchez la Stegomyia!*[1] (See fig. 85.)

For a long time it was thought that yellow fever was induced by a filtrable virus, an ultramicroscopic organism. But recently Noguchi has forged what appears to be the last link in the chain of evidence which establishes that the organism called "*Leptospira icterohæmorrhagiæ*" is the cause of yellow fever. (See fig. 86.) It is an extremely delicate spirochaetal filament, which moves as rapidly as though equipped with a propeller, even though it has no terminal flagella. At great pains Noguchi not only observed this organism in the blood of yellow-fever patients, but succeeded in infecting guinea-pigs and finally in growing *Leptospira icterohæmorrhagiæ* on a special semi-solid medium. Noguchi succeeded in preparing serums which promise to be of great value in the treatment and prevention of yellow fever. But in studying African yellow fever, which differs from the familiar South American form, on the Gold Coast in 1928, this distinguished scientist succumbed to the former disease, although he had taken serum as a preventive against the South American form in the hope that it might also protect him in Africa. In Noguchi, bacteriology has suffered an irreparable loss.

FIGURE 85

The yellow-fever mosquito, Stegomyia. At the left, male; at the right, female. (After Conn and Conn.)

The chief method of prevention of the disease is, of course, the safeguarding of houses against the entrance of the mosquito *Stegomyia fasciata* (*Aedes ægypti*) and its eradication. Gorgas's great work in this connexion in cleaning up the Panama zone has been heralded throughout the world. White did as much for New Orleans in 1905 when after a vigorous campaign he ac-

[1] Now known as *Aedes ægypti*.

complished the rare feat of making it difficult to find a stegomyia mosquito in the largest city of the South. Oswaldo Cruz performed the same service for Rio de Janeiro in 1909. Careful screening of yellow-fever patients and suspects, extermination

FIGURE 86

Leptospira icterohæmorrhagica, the cause of yellow fever. (After Noguchi in the "Journal of Experimental Medicine.")

of stegomyia mosquitos by insecticides and fumigation, and eradication of breeding-places form the bulwarks of yellow-fever prevention.

Yellow fever has terrorized mankind for centuries. It will do so no more, for it has been conquered. Bacteriology boasts few more heroic achievements.

Chapter XVIII

BEYOND THE MICROSCOPE

Bacteria are of all sizes, ranging from small cocci to large spirochætes, yet there are many species scarcely discernible, or which defy definition even by the microscope. The name "filtrable virus" is applied to this rather large group of very important organisms, which make up in virulence what they lack in size. The term "filtrable virus" is in a way a confession of ignorance. It implies that we know little concerning the character of the organism in question beyond the fact that it is exceedingly small and that it will pass through clay and unglazed porcelain, which ordinarily act as normal filters in restraining the passage of bacteria through their pores. (See fig. 26.) Again, in comparison with bacteria, it is extremely difficult to cultivate filtrable viruses artificially or to stain them satisfactorily. The classification of filtrable viruses is arbitrary and therefore frequently open to criticism upon technical grounds, such as the acidity or alkalinity of the medium being filtered, the electrical charge on the filter, etc. Until more exact ultramicroscopic methods are developed, the status of the filtrable viruses must remain equivocal.

The question might well be raised: How do we know that diseases are caused by filtrable viruses when the latter cannot be accurately described? The answer is simple. The same symptoms and disease can be produced by inoculation and subinoculation into an indefinite number of animals. It might be ventured in rebuttal that the injection of a poison may also produce similar symptoms. Aside from the fact that a definite period of incubation is required for diseases due to micro-organisms compared with the rather sudden onset of symptoms following chemical poisoning, the most important feature is that any poison introduced into an animal would upon successive passage from this animal to other animals result in dilution, the original poison

becoming so diluted that it would ultimately have no effect. On the other hand, we know that we are dealing with living organisms, although they are unseen, when after many successive transfers from individual to individual they lose none of their power to produce disease, but in most cases this power is actually *enhanced*.

I. SMALLPOX

Smallpox, or variola, requires no introduction. It has been one of the worst of epidemic diseases — known to China and other countries of the Far East long before the Christian era; raising havoc with the crusaders in the Middle Ages; and terrifying the uncivilized communities of today. It is only poetic justice that Columbus's sailors took syphilis back to Europe with them, for the Spaniards are considered responsible for the introduction of smallpox into this country.

It has been estimated that sixty million people died of smallpox during the eighteenth century alone. Catlin states that, of twelve million American Indians, six million have fallen victims to smallpox. When one stops to add up the appalling number of deaths from smallpox, plague, cholera, and other epidemic diseases, one may well wonder how it is that there are still enough human beings left to populate the earth. The survivors can be grateful for the fact that resistance to disease, or immunity, is so individual a matter.

Thanks to vaccination and rigid quarantine regulations, smallpox has been almost entirely eradicated from modern civilized society. Outbreaks still occur, even in the United States, but they usually originate in those parts of the country where vaccination is not so widely practised as it should be. Death, or disfiguration for life, is a stiff price to pay for neglect or for belonging to a cult that cannot be convinced of the value of vaccination. Despite G. B. Shaw, who never loses an opportunity to level shafts of criticism against vaccination, and other less literary folk, the world's statistics carry convincing proof of the reduction of mortality from smallpox by vaccination.

There are three forms of smallpox, according to Osler: *variola vera*, *variola hæmorrhagica*, and *varioloid*. The first form, true smallpox, is characterized by a chill in adults or a convulsion in

children, severe headache, vomiting, sharp pains in the back and limbs, fever, and even delirium. There is a skin eruption, which is either discrete, the pustules standing out separately; or confluent, the pustules running together. The typical smallpox vesicle is a dome-shaped blister containing at first a clear fluid and later pus. A depression forms in the middle of the blister, which looks for all the world like the umbilicus. Eventually the pustule dries up and forms a crust. Of the second form, hæmorrhagic smallpox, there are two types: black smallpox, which is usually fatal, in which the skin becomes purplish and there is bleeding of the mucous membranes; and *variola pustulosa hæmorrhagica*, in which the pustules, or pocks, fill up with blood. The mucous membranes also become bloody. In most cases the disease in this form is fatal. The third form, varioloid, is the modified form of the disease which occurs in vaccinated persons. All symptoms are usually milder than those in unvaccinated individuals.

While the cause of smallpox remains unknown, there is ample proof that it is an infectious disease, easily transmitted by direct or indirect contact. Various theories have been advanced as to the nature of the causative agent, but none has proved convincing. Protection against smallpox, however, is soundly established. Jenner (see fig. 87), whose name is famous in the annals of bacteriology, became familiar with the tradition of the country people in Gloucestershire that anyone who had been infected with cowpox was usually immune from smallpox. In fact, it was a milkmaid who first apprised him of this fact, which seemed to him to have tremendous possibilities. He consulted the great surgeon Hunter, who told him: "Don't think, try; be patient, be accurate." Whereupon he performed the practical experiment of inoculating a boy, James Phipps, with pus taken from a cowpox pustule on the hand of a dairymaid who had the disease. The same boy two months later (this was in 1796) was inoculated with material taken from a smallpox pustule. He did not contract smallpox. Thus were the principles of smallpox vaccination established. To show his appreciation, Jenner built a cottage for Phipps and planted the roses in the garden with his own hands.

The difference between cowpox and smallpox is difficult to

establish, for they are closely related. Not so with chicken-pox, which is distinct from and cannot protect against smallpox. There is another disease, alastrim, occurring in epidemic form in the tropics, which resembles smallpox so closely that it is considered to be a mild variety of smallpox.

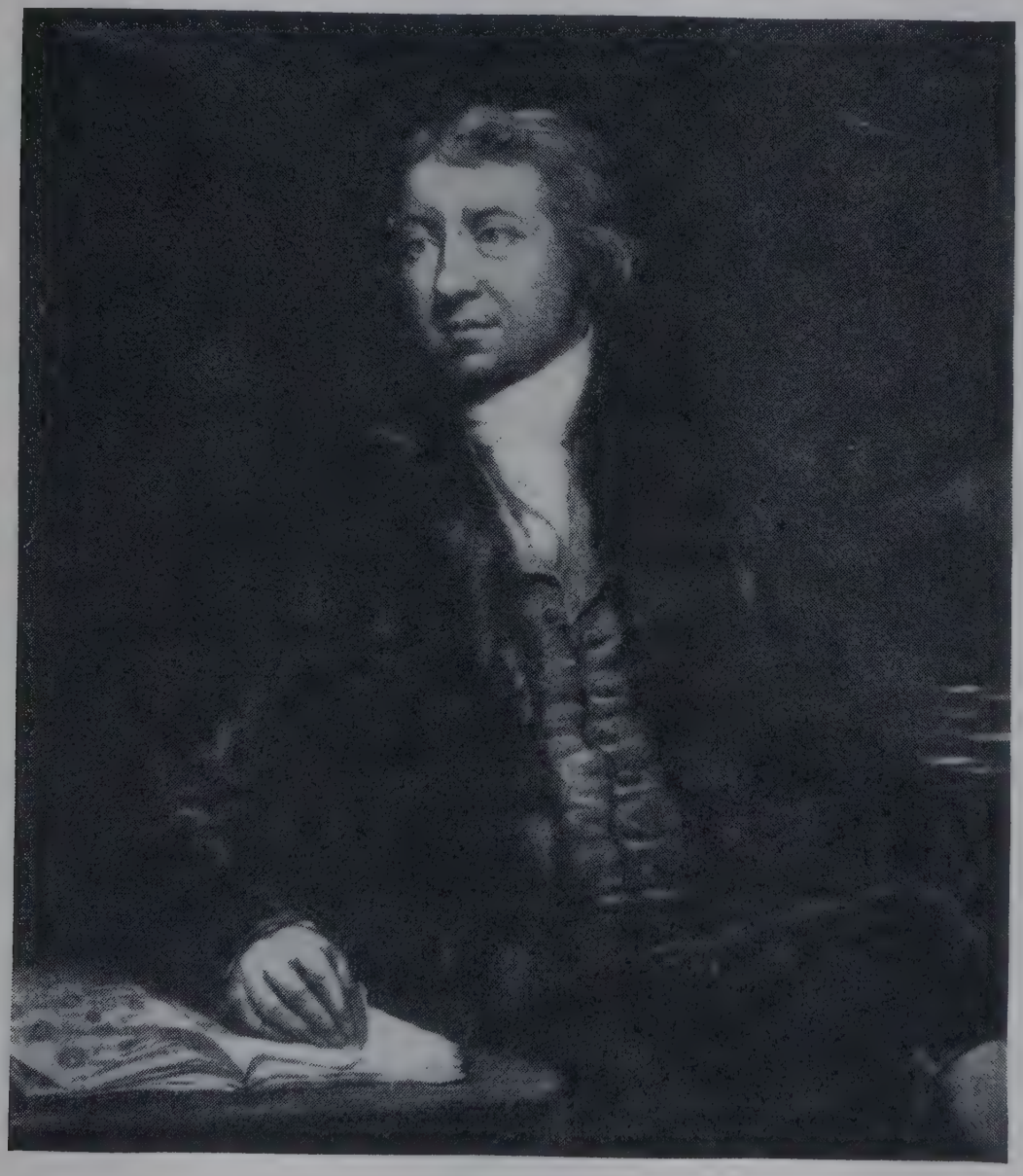


FIGURE 87

Jenner, discoverer of vaccination for smallpox. (New York Academy of Medicine.)

The actual methods for preparing smallpox vaccine will be described later. Suffice it to say that the usual method is to inoculate calves with cowpox and permit them to develop typical pustules. From these the pulpy exudate is collected and the vaccine virus used to vaccinate human beings.

Vaccination, as is well known, consists of rubbing the vaccine

virus into a surface scratch, or injecting it into the skin.[1] If the vaccination "takes," a scab is formed. If not, the procedure should be repeated several times to be sure that the individual is immune. The blister which forms immediately after vaccination has been glowingly described as "the pearl on a rosebud," and the scar which is left, "a sanitary dimple." Babies should be vaccinated as soon as possible and before they are eight months old. Vaccination ought to be repeated every seven years, or oftener if there is an epidemic.

Statistics comparing the mortality from smallpox before and after the introduction of vaccination are striking. Thus in Sweden for twenty-five years before the introduction of vaccination there were 2,050 deaths from this disease, or a death-rate of 20 per million inhabitants. In the *thirty-five years after vaccination* was enforced, there were only 169 deaths or a death-rate of 0.17 per million inhabitants, which is a decrease of more than ninety per cent. Osler says: "Communities in which vaccination and revaccination are thoroughly and systematically carried out are those in which smallpox has the fewest victims. The German army since 1874, the date of the stringent laws, has enjoyed practical immunity. On the other hand, communities in which vaccination and revaccination are persistently neglected are those in which epidemics are most prevalent. Owing to a widespread prejudice against vaccination in Montreal, there grew up, between the years 1876 and 1884, a considerable unprotected population, and the materials were ripe for an extensive epidemic. The soil had been prepared with the greatest care, and it only needed the introduction of the seed, which in due time came with the Pullman-car conductor from Chicago on the 28th of February, 1885. Within the next ten months thousands of persons were stricken with the disease and 3,164 died." Osler or Shaw — yours is the choice!

[1] The term "vaccine virus" refers to the agent which causes cowpox, "vaccinia." The root, "*vacca*" (meaning cow), enters into "vaccinia" and "vaccination." In other words, during vaccination we introduce the virus which causes cowpox as a protection against smallpox.

2. MEASLES

Measles is one of the most common of infectious diseases and is confined to man alone. Essentially a disease of childhood, it has also been known to attack adults, causing epidemics among the more uncivilized peoples. Is it, then, altogether a paradox that colleges boast of measles epidemics? Measles is responsible for one per cent of all deaths occurring in the temperate zones and it has been estimated that there are more than ten thousand deaths from measles each year in the United States. The disease is universally known; in fact, it is the prevailing opinion that everyone must contract the disease. Of course it is true that almost everyone does, but this need not be so if proper precautions are observed.

The symptoms of measles are familiar: sneezing, running nose, reddened eyes, cough, fever, and a rash about the fourth day. One of the earliest and surest diagnostic signs in measles is the presence of "Koplik's spots." These are white or bluish-white specks, surrounded by a circular red coloration at the bases of the lower milk molars. Measles itself is not greatly to be feared, but the complications of throat affections, pneumonia, rheumatic conditions, and nervous manifestations are serious. It is during convalescence that extreme care should be taken of the patient to prevent his or her catching cold, otherwise the way is paved for lung infections, such as pneumonia or tuberculosis. Since it takes four days for the symptoms to develop, there is ample opportunity for transmitting the disease. This makes constant inspection of schoolchildren most important. Those with colds should be segregated. This vigilance has proved valuable not only for schoolchildren, but for adults as well, as army experience and factory supervision have demonstrated. The disease is readily communicated by secretions from the nose and throat and probably by contaminated objects, such as toys or clothing.

The cause of measles is still unknown, although there seems to be an increasing body of evidence which indicts a streptococcus, as in scarlet fever, which for a long time was thought to be caused by a filtrable virus. Unfortunately there has been no vaccine developed which is comparable to that used in smallpox.

Recently, however, promising results in treatment have been obtained by the use of convalescent serum. In other words, the injection of serum from the blood of patients who are recovering from an attack of measles protects against the disease in from fifty to seventy-five per cent of cases. It also alleviates symptoms, causing the disease to take a milder form when used early in the course of the disease.

German Measles (rubella) is a milder infection, similar in most respects to measles.

Mumps is another disease caused by a filtrable virus which is responsible for numerous epidemics. Chiefly a disease of children, it has been known to raise havoc among adults in army camps and colleges. The swelling in front of and below the ear is characteristic. The salivary glands and testicles are frequently inflamed. One simple but ingenious diagnostic test, really a psychological test, is to present a lemon to the sight of a patient in whom mumps is suspected. If the salivation resulting from such a visual stimulus is scanty and painful, then it is concluded that mumps is responsible for the inflammation which has blocked the salivary glands.

As with measles, the disease is readily communicated. Rigid inspection and isolation are imperative in checking its spread; also convalescent serum appears to protect against the disease.

3. HYDROPHOBIA OR RABIES

Possibly a barking dog does not bite, but beware the bite of a dog frothing at the mouth, whether he barks or not, for he may give you hydrophobia, or rabies. The dog is not the only animal carrying this disease; as a matter of fact, many warm-blooded animals, such as cats, wolves, and skunks harbour the virus. Man becomes infected when saliva from a rabid animal enters a bite or a scratch. Rabies is common in Russia, France, and many other countries, including the United States. But it has been practically eradicated from England and northern Germany as a result of stringent laws concerning muzzling and importation. There is today no possible excuse for the occurrence of rabies in civilized communities, for dogs can be so muzzled that it becomes impossible for them to bite human beings. What is wanted is

more humanity to man and less sentimentality towards dogs. Particularly is this so since children are most likely to be bitten when a rabid dog is on the war-path. Adults can make their escape more easily.

Following the bite of a rabid animal, a considerable period of time elapses before the symptoms of rabies set in — usually this incubation period, which is variable, is from six weeks to two months. About one-third of those bitten by rabid dogs contract rabies if allowed to go untreated and the mortality is about thirty-five per cent. The extent of the bite is a determining factor; for often clothing may prevent the entrance of saliva into a superficial bite. If symptoms are allowed to develop, there is only one outcome — death. The disease is characterized by depression; headache; pain in swallowing, especially water, the very sight of which causes dread, hence the name "hydrophobia" (fear of water); a period of intense excitement; delirium; and finally paralysis, ending in death.

FIGURE 88

Above, normal brain cell. Below, the same with two Negri bodies. (After Conn and Conn.)

Pasteur's discovery in preventing the development of rabies will remain one of his greatest achievements. By drying the spinal cords of dead rabid animals Pasteur attenuated the virus. It could then be injected into other animals in increasing amounts so that finally the bite of a rabid animal would prove innocuous to the animals protected by inoculation. Many attempts have been made to cultivate the virus artificially, but none is universally recognized. The filtrable virus of hydrophobia proves elusive, even though it contains so-called Negri bodies, which resemble protozoa. (See fig. 88.)

It was a great day for Pasteur and for humanity when Joseph Meister was brought to him to be saved from the inevitable death of rabies. Pasteur inoculated him as he did his animals and saved his life. According to Högyes, fifty thousand victims were successfully treated in a ten-year period, with an average mortality of only one per cent. To achieve these results many animals have had to be sacrificed. Do not embarrass the antivivisectionists by asking whether this is worth while. The Pasteur treatment

FIGURE 89

The Pasteur Institute in Paris.

is now practised successfully the world over and the Pasteur Institute in Paris is the living testimonial of a grateful public. (See fig. 89.)

4. INFANTILE PARALYSIS AND SLEEPING-SICKNESS

Infantile-paralysis epidemics are increasing in number in recent times, especially in the United States. The technical name for this disease, which attacks the younger members of the community, particularly below the age of five, is "acute anterior poliomyelitis," so called because it is localized in the front horns of grey matter in the spinal cord. The disease takes various forms, with symptoms resembling cerebrospinal fever, influenza, or certain gastro-intestinal disorders. A typical case is described by Morse:

"Fred C., seven and one-half years old, had always been well except for measles and whooping-cough some years before. He

had been spending the summer in a locality within twenty miles of which there had been several cases of infantile paralysis during the past few weeks. He complained of headache the afternoon of September 7. He vomited and was somewhat feverish the next morning but went in bathing that noon as usual. He complained in the evening that his throat felt a little full. He was given a laxative that night and had a good movement the morning of the ninth. He was brought home that day by train, a journey of about one hundred and twenty-five miles. He took a little milk and ate several crackers on the way. He walked out of the station to his automobile without difficulty. He undressed himself and ate a little supper, although he complained that it was hard for him to swallow. He was seen by his physician in the early evening. The physical examination, including the throat, showed nothing abnormal. His mouth temperature was 103°F., his pulse 115, and rather feeble. He collapsed about midnight and was seen again soon after by his physician. He was then slightly cyanotic [bluish]. His pulse was very feeble and his respiration rapid. He was unable to swallow anything, not even his saliva. . . . Respiration was entirely diaphragmatic. There was no movement of the chest wall and the accessory muscles of respiration were not acting." A diagnosis of infantile paralysis was made and little hope was offered.

Paralysis of the limbs with characteristic irregularity may set in abruptly or there may be symptoms of the bulbar form, which begins with paralysis of the eyes, face, or throat. The disease usually results in deformities of the leg. The mortality rate of infantile paralysis, fortunately, is not high. Osler gives it as from four to fifteen per cent.

The cause of infantile paralysis is still a matter of debate, and more conservative opinion holds to a filtrable virus. Flexner and Noguchi, however, claimed to have isolated very minute globoid bodies from the virus and to have cultivated them artificially in the same medium used successfully for the growth of *Spirochæta pallida*, the cause of syphilis. Experimentally, the virus of infantile paralysis has been transmitted to animals, chiefly monkeys. Animals which recover after such injections are immune from further attacks of infantile paralysis, as are human beings who recover from an attack of the disease, and the serum from

such individuals has been used to protect incipient cases, particularly in the first few days of the illness, before paralysis sets in. The diagnosis of infantile paralysis is very difficult in the earliest stage of the disease.

An accurate diagnosis is likely to be made much more frequently during epidemics, when physicians are on the watch for the disease or when public health bureaux are so organized that the practising physician may have the benefits of consultation with experts. For this very reason it is far better for a child to contract the disease during an epidemic than at other times, when the diagnosis is likely to offer difficulties.

Progress in the treatment of the disease by surgical and other methods has been so great that at the present time deformities can be prevented and the use of cumbersome apparatus made unnecessary.

There are several theories to account for the transmission of the disease, the most plausible being that the virus is discharged from the mouth and nose of the infected patient and infects others through the same channels. It seems probable that insects, such as stable-flies, may help to spread the disease. In view of the present limited knowledge concerning the disease there is little that can be done in the way of prevention beyond the usual sanitary measures.

Sleeping-sickness is, in a sense, a misnomer for *encephalitis lethargica*, because originally the name was applied to African sleeping-sickness, caused by a trypanosome (to be described later); and further because the disease is almost as frequently characterized by extreme restlessness and irritability as by lethargy. Curiously, sleeping-sickness epidemics are almost always preceded by influenza epidemics, and mistakes in diagnoses of these two diseases are not uncommon. Sleeping-sickness occurs most frequently in young adults and resembles infantile paralysis in many respects. The symptoms are variable, including: headache, somnolence, coma, delirium, restlessness, irritability, and vomiting. The patient frequently sees everything double. Paralysis of the face and muscles may ensue.

In sleeping-sickness complete recovery does not often occur and the acute stages just described are likely to develop into a chronic condition in which the manifestations of the disease are

protean. Thus a very common picture is one closely resembling shaking palsy. The patient develops a rigid, expressionless face, a tremor of the head and extremities, and a peculiar lack of flexibility of the joints. The physical movements are those of a wax figure. Such a condition may lead the patient into a state of complete helplessness. The movements are so slow and awkward that the patient permits saliva to drool from his lips rather than take the trouble to close his mouth. Mental retardation frequently corresponds in degree to physical retardation. Further, mental aberrations may take place, particularly in childhood. Behaviour may become abnormal. Thus boys go "bad," apparently quite suddenly, and fall into the hands of truant officers or others. Sometimes even insanity ensues.

As in infantile paralysis, the cause of sleeping-sickness is believed to be a filtrable virus, the exact nature of which remains undetermined. Loewe and Strauss, however, have described minute globoid bodies, much like those which Flexner and Noguchi consider to be the cause of infantile paralysis.

Apparently the disease is transmitted by the direct contact with nasal and throat secretions, as in infantile paralysis. Similarly, there is little knowledge concerning prevention.

Cold sores or fever blisters (*herpes febriles*), the fairly common eruptions about the lips and face, are caused by a filtrable virus very closely allied to that of sleeping-sickness.

There are many other filtrable-virus diseases of man, not so widely known as those here described:

Trachoma — the contagious inflammatory eye-disease against which immigration authorities guard painstakingly, because of the blindness which usually follows — has always been considered to be caused by a filtrable virus. Trachoma is relatively infrequent in the United States, and when it does occur, it is found chiefly among the native Indians on the governmental reservations. Recently Noguchi claimed to have discovered a bacillus as the real cause of this disease. Noguchi also recently described the causal agent of Oroya fever and *verruga peruviana* — two South American febrile diseases, transmitted by gnat-bites.

Dengue fever, another tropical febrile disease, is caused by a filtrable virus and shown by Siler, Hall, and Hitchens to be

transmitted by the bite of the same mosquito (*Aedes ægypti*) that transmits yellow fever.

Pappataci fever, known as "three-day fever," which is transmitted by the sand-fly, occurs chiefly about the Mediterranean and in warm climates.

Molluscum contagiosum is a contagious skin-disease characterized by knob-like growths.

5. FILTRABLE-VIRUS DISEASES OF ANIMALS AND PLANTS

There are a number of diseases of animals and plants which are caused by filtrable viruses. Among these may be mentioned:

Foot-and-mouth disease, characterized by skin eruptions in the mouth and on the hoofs of cattle, sheep, or goats. The economic loss from epidemics of this disease is enormous. It is estimated that there was a loss of almost six million dollars in the United States alone from October 1914 to May 1916. The disease is rarely transmitted to man, and causes only a very mild infection.

Hog cholera, another important epidemic disease, for a long time believed to be caused by a member of the group of paratyphoid bacilli.

Peripneumonia of cattle, characterized by pleurisy and pneumonia, epidemic in nature. It is caused by a filtrable virus transmitted by contact.

Cattle-plague, or rinderpest, a fatal disease of cattle characterized by inflammation of the mucous membranes, particularly of the nose and intestinal tract.

Catarrhal fever of sheep, or "blue tongue," a serious disease, of economic importance in South Africa.

Agalactia of sheep and goats, a disease which affects the secretion of milk in these animals. It is of economic concern in Italy and the lower Alps.

Cowpox, a pustular disease of cattle closely resembling human smallpox in every particular.

Sheep-pox, a disease of sheep closely resembling smallpox and cowpox.

Fowl-pox, a similar disease of fowls.

Fowl plague, a disease of chickens in which they become weak and sleepy, the comb turns violet, and death usually occurs within a few days.

Chicken diphtheria, a disease so much like fowl plague as to be practically indistinguishable from it.

Leukæmia of chickens, closely resembling the human disease, in which there are marked blood changes, notably an increase in the number of white blood cells.

Chicken sarcoma, characterized by tumours in chickens resembling those found in man.

Lymphosarcoma of dogs, a sexually transmitted tumour occurring about the genitals of dogs.

Canine distemper, a common disease in young dogs, characterized by fever, severe catarrh, and inflammation of the respiratory passages. It is generally considered to be caused by a filtrable virus, although some investigators, notably Ferry, have described an influenza-like bacillus as the causal agent.

African horse-sickness, an epidemic disease which kills many horses, mules, and donkeys.

Pernicious anæmia of horses, a disease characterized by fever during the day, which drops at night, swelling of the head and neck, reddish frothing at the mouth, and a decrease in red blood cells. The filtrable virus causing this disease may be recovered from either blood or urine.

Guinea-pig paralysis, a disease somewhat resembling infantile paralysis in man.

Rivers's rabbit disease, a spontaneous disease in rabbits, causing inflammation of the skin and eye, found by Rivers during the experiments dealing with the transmission of chicken-pox.

Silkworm jaundice, a skin disease of caterpillars, characterized by swelling, yellowing, and drying.

Mosaic disease of plants, a fatal disease of tobacco, tomato, potato, and other plants, in which the leaves become mottled and curl up. It is of considerable economic importance. Olitzky has done much towards establishing the filtrable-virus nature of this disease.

The diseases enumerated in this chapter form a group which, pending further study, are considered to be caused by filtrable viruses. There are investigators who claim to have discovered the

causal agent of this or that disease, but final proof or confirmation is wanting. The group of filtrable-virus diseases, therefore, represents a scientific scrap-basket from which valuable material may yet be plucked. More refined methods of examination and artificial cultivation will some day make necessary a reclassification of these diseases.

Chapter XIX

TYPHUS FEVER AND OTHER INSECT-BORNE DISEASES

I. TYPHUS FEVER

Typhus fever, not to be confused with typhoid fever, takes rank with the great epidemic diseases, which are inscribed on those dark pages which recount the grievous visitations of mankind by war, famine, and misery. Great Britain (particularly Ireland), Europe, and Asia have been ravaged by this disease, which is intimately associated with filth and overcrowding. In Dublin alone in 1846 sixty thousand persons died of typhus fever.

Typhus fever has as many aliases as a gunman. In New York typhus fever has gone by the name of "Brill's disease"; in Mexico it is called "tabardillo." It has also been called: "hospital fever," "spotted fever," "jail fever," "camp fever," and "ship fever."

It is an acute disease, characterized by sudden onset, rise in temperature, pink rash, cough, and nervous symptoms, sometimes culminating in delirium. Complications are greatly to be feared. They may include middle-ear infections, bronchitis, gangrene of the extremities, and paralysis.

To put it bluntly, typhus fever is transmitted entirely by lice. This was proved by Nicolle in 1909 and has been amply confirmed subsequently. So ingenious are the methods employed by scientists in the study of infectious disease that one distinguished American bacteriologist engaged in the study of typhus fever used himself as a source of food for some pet lice. He carried these live creatures from the United States to Poland by strapping to his bare leg a box containing the lice. They were thus able to bite his leg, suck the blood, and remain alive for experimental purposes. They were in such a healthy condition when Poland was reached that they were able to bite typhus-fever patients. Then the intestinal tracts of these insects were carefully examined in an effort to find the causal agent of typhus fever.

It is believed by some investigators that the head-louse as

well as the body-louse may transmit the disease. Is it any wonder, then, that typhus-fever epidemics flourish in the presence of filth, overcrowding, poverty, and war? Where bathing is a luxury, typhus is a common occurrence. The epidemic which occurred in Serbia at the beginning of the World War, as described by Strong, is a perfect illustration. As a result of fighting the Austrians in the north, the Serbian civilian population had to flee south. Scanty clothing, infrequently changed, inclement weather, inadequate shelter, insufficient food, overcrowding under the filthiest conditions, all made an ideal soil for the development of typhus fever. At the height of the epidemic, there were reported nine thousand cases daily, with a mortality of thirty to sixty per cent. It was estimated that one hundred and fifty thousand persons died from typhus fever in Serbia within six months. This makes it easy to understand why the Austrian Army delayed its second attack upon Serbia; Austria knew well that Serbian lice would create greater havoc than Serbian rifles.

The cause of typhus fever is one of the most puzzling of bacteriologic problems. Whether a filtrable virus is responsible for the disease, or an organism too large to pass through the ordinary laboratory filters, remains a matter of debate. Various bacilli, notably that discovered by Plotz, and protozoon-like bodies, called Rickettsia bodies, have been held responsible for it.

There is a specific serum test for typhus fever, called the "Weil-Felix reaction," which is of importance in identifying the infection. It depends upon the agglutination of an organism belonging to the *Bacillus proteus* group. In other words, in the proper dilution the Proteus organisms in a pure culture will agglutinate or clump when serum from a patient with typhus fever is added. This is an important diagnostic test, similar to that employed in typhoid fever, yet entirely distinct. No successful vaccine such as is used for the prevention of typhoid fever has as yet been devised for typhus fever, chiefly because the causal organism still evades identification. The prevention of typhus fever, consequently, must depend upon personal and public hygiene, with particular emphasis on the extermination of lice.

2. TRENCH FEVER

Trench or Volhynia fever was prevalent on the German front and in Volhynia at the beginning of the World War. The disease is characterized by a sudden onset, resembling influenza, accompanied by headache, fluctuating or "spiky" temperature, and pains in the muscles and joints. Relapses are likely to be of frequent occurrence. Whether the disease is caused by a filtrable virus or by Rickettsia bodies is an open question, but that the disease is transmitted by lice is certain. Human volunteers have established this important conclusion, just as in yellow fever. To quote Zinsser: "Careful experiments were made with lice, all of which were reared from eggs and fed on normal subjects and the non-infectiousness of these lice was proven by allowing them to feed on eleven different uninfected people. Such lice were allowed to feed several times on trench fever patients and subsequently allowed to feed on twenty-three volunteers, 78 per cent of whom developed trench fever. It did not seem necessary for the lice to be in contact with the skin while feeding, nor was it necessary to produce scarification. In two instances the mere bite of the louse through the meshes of gauze covering the box produced the disease. . . . Prevention of trench fever, like the prevention of typhus, depends upon delousing."

3. ROCKY MOUNTAIN SPOTTED FEVER

Rocky Mountain spotted fever is a disease long known to the mountains of Montana and Idaho, with an especially high mortality in certain localities. The symptoms resemble those of typhus fever, just described. The disease is transmitted by the wood tick, *Dermacentor venustus*. The causal organism appears to be a minute double coccus, resembling the Rickettsia bodies of typhus fever. Recently Noguchi claimed to have isolated the *Bacillus rickettsiformis* as the offending microbe. As with other insect-borne diseases, the prevention of Rocky Mountain spotted fever lies in the eradication of its disseminator, the wood tick. But this is likely to prove a difficult and impracticable procedure. Even lice, which occur ubiquitously, may be more easily guarded against.

Since in the transmission of typhus and trench fever lice are so important, a few facts concerning them should be of interest. The lifetime of a louse is about a month to six weeks. It lays its eggs by choice on the inner surface of underclothing, wearing-apparel, blankets, etc. The adults feed about twice a day. Without a ready source of food the louse, as might be expected, dies of starvation. To the occasional and unwilling victim the bite of the louse is decidedly an uncomfortable experience; to the habitué it is unnoticeable.

Delousing of the individual is best accomplished by repeated hot baths, with a liberal use of soft soap. The clothing must be rigidly inspected and treated with some organic compound like creosote oil, naphthaline, or kerosene. Rooms and clothing may be disinfected by the use of hot air or steam under pressure, or sulphur dioxide gas. Much valuable experience was gained during the World War in the control of lice.

Lice have been found to harbour in their intestinal tract minute oval bodies, called "Rickettsia," named after Ricketts, who has done much important work on them. Rickettsia bodies resemble very small bacilli or protozoa. They are to be found in typhus, trench, and Rocky Mountain spotted fevers. They are difficult to stain, Gram-negative, and non-motile and require an insect host for transmission. Wolbach has classified a number of Rickettsia, some producing disease and others of no particular concern to man. Until they can be cultivated artificially, knowledge concerning them must necessarily remain limited.

Chapter XX

BACTERIOPHAGE

The microscope makes visible a host of minute living organisms, the bacteria, which play an important rôle in disease, in agriculture, and in industry. But there are bacterial phenomena, as we have seen in the filtrable viruses, which lie beyond even the microscope. None is more fascinating than the bacteriophage — "bacteria-eater." Are there really living organisms more minute than bacteria which feed upon them, or are bacteria destroyed by some more insidious agent?

Whatever the explanation, the fact remains, and it has been repeatedly observed by many investigators, that bacteria have, as it were, been eaten alive. While various aspects of this phenomenon have been familiar, it remained for Twort in 1915 to describe bacteriophage in its entirety. Further, he suggested a theory, which is similar to that of d'Hérelle, whose name is most frequently associated with bacteriophage. Twort regarded bacteriophage from the standpoint of an infectious disease of bacteria; d'Hérelle pointed out its importance in relation to the diseases of man.

According to d'Hérelle, bacteriophage is a living autonomous ultramicroscopic organism invading bacteria, multiplying, and causing the bacteria to burst. In other words, bacteriophage is a parasite on bacteria, just as bacteria are parasitic on human blood-cells. It recalls the rhyme:

> Great fleas have little fleas
> Upon their backs to bite 'em
> And little fleas have lesser fleas
> And so *ad infinitum!*

(De Morgan)

It is interesting to follow d'Hérelle's train of thought in arriving at the phenomenon of the bacteriophage. He observed that during a patient's recovery from an attack of dysentery the offending dysentery bacilli disappeared from the stools. What

caused this disappearance? He inferred that the stools must contain a substance which either inhibits or destroys the dysentery bacilli. Experiments in the laboratory showed that upon introducing small amounts of stool suspension or filtrate into dysentery cultures, the dysentery bacilli were dissolved or "lysed." When a trace of this dissolved culture was introduced into a fresh culture of dysentery bacilli, the same phenomenon of dissolution or lysis occurred. And this was continued throughout a series of 935 passages! D'Hérelle therefore concluded that the lytic principle originally present must have multiplied, else how could it be sufficiently active to produce such results after repeated passage and dilution?

Another feature of bacteriophage was brought out upon examination of streaked plates (solid nutrient medium upon which the dysentery bacilli were grown in parallel lines). It was noted by d'Hérelle that there were discrete, dissolved spots, which suggested that the lytic principle was distributed in units — was, in a word, particulate.

Finally, it was d'Hérelle's belief that bacteriophage secretes an enzyme, or substance which promotes chemical activity, to such an extent as to cause a destruction of the bacterial cell attacked. We know, for example, that proteolytic enzymes will destroy proteins, which are important constituents of the bacterial cell.

Thus, summed up, d'Hérelle's conception of bacteriophage is that: it multiplies; it is particulate; and it secretes an enzyme. All these are properties of living and not of inanimate matter; consequently, he believes that bacteriophage is a living thing. Further, he holds that bacteriophage has the power of adaptation, another function of all living organisms. Bacteriophage may be adapted to any and all bacteria; it is general and not specific in character. Moreover, like all living things that have the capacity of adaptation, it can acquire a tolerance for poisons or injurious agents. Just as man succumbs to a large initial dose of morphine, but can acquire a tolerance for morphine by a gradually increasing dosage until the dose that would originally have killed him proves innocuous, so bacteriophage ordinarily killed by a large dose of poison can develop a tolerance enabling it to survive an otherwise fatal dose.

The actual observations on bacteriophage described by

Twort and d'Hérelle have been amply confirmed by numerous bacteriologists — it is the interpretation of the phenomenon which remains open to discussion. The conflicting theories can be conveniently grouped under two headings: (1) endogenous — that is, bacteriophage as a product of bacteria; (2) exogenous — that is, bacteriophage as an entity coming to the bacterial cell from without. Obviously, into the second category, based on the exogenous nature of bacteriophage, fall the major contributions of d'Hérelle and his followers. The first category, based on the endogenous nature of bacteriophage, may be further subdivided — namely, (a) bacteriophage simply as an agent or activator which speeds up bacterial fermentations (enzymic); and (b) bacteriophage as a product of the life-process of bacteria (metabolism), which product kills the bacteria themselves, just as man would succumb to his own excretions if provision were not made for their removal.

It is the latter thought which has developed out of the research by Bronfenbrenner [1] and his co-workers at the Rockefeller Institute. It was shown by them experimentally that bacteriophage, unlike a living organism, *does not respire*. Again one of the chief constituents of living matter is protein; and either bacteriophage contains no protein at all, or, if it contains any, it is present in such small amounts, even in concentrated material, as to be utterly negligible as a factor in its composition. We have here strong evidence against the theory that bacteriophage is a living organism.

D'Hérelle considered bacteriophage universal because the bacteriophage from one kind of bacillus dissolved other kinds of bacilli upon repeated passage. Present knowledge holds this view to be incorrect. In other words, it has been demonstrated that there is only one specific bacteriophage for each particular type of bacteria and that this specific bacteriophage cannot be adapted to other types of bacteria, just as the diphtheria bacillus causes diphtheria and not tuberculosis. Any apparent universal adaptability of bacteriophage is due rather to a mixture of different bacteriophages than to a universal bacteriophage. Similarly, it was supposed by d'Hérelle that a serologic test

[1] Thanks are due to Dr. J. J. Bronfenbrenner for the material furnished for this chapter.

known as the "complement-fixation test" established the universality of bacteriophage, but more recent investigation indicates that different bacteriophages yield specifically different and not similar reactions.

The apparent multiplication of bacteriophage, upon which d'Hérelle laid great emphasis, does not seem to rest on a secure basis. While it is true that bacteriophage is present in a medium in a state of indivisible units, these units are probably not autonomous, but adhere to the particles of medium which carry them. The greater the multiplication of bacteria present in the medium, the greater the quantity of bacteriophage. In other words, it appears that bacteriophage is quantitatively dependent upon the growth and multiplication of the bacteria with which it is associated.

D'Hérelle claimed that there is an enzyme secreted by bacteriophage which like all enzymes is completely precipitated by ten volumes of alcohol. But Bronfenbrenner has shown that such inactivation is not complete, that some of the lytic principle escapes in sufficient amount to cause lysis in the second generation — whereas d'Hérelle states that lysis can occur only in the first generation after such an alcoholic precipitation. Therefore, the notion that the action of bacteriophage depends upon an enzyme which can be precipitated by alcohol is open to question.

Finally, the interesting point that bacteriophage is a living thing because it can acquire a tolerance for injurious agents is ingenious, but not conclusive. Many analogous examples can be cited from the field of colloidal chemistry, which deals exclusively with non-living phenomena.

What, then, is bacteriophage? There have been many theories advanced to explain the phenomenon, some highly hypothetical and incapable of proof; others plausible to a degree, yet lacking in experimental evidence. From Bronfenbrenner's investigations he was led to conclude that it is an *intracellular product of normal bacteria*. In other words, it is a by-product of the bacterial life-process, or metabolism. During the stages of rapid multiplication of bacteria it is conceivable that the membrane which surrounds a bacterial cell becomes more permeable, permitting the escape of bacteriophage.

The principal features of the bacteriophage phenomenon are

that: it stimulates the growth of bacteria; it causes a more rapid multiplication of bacteria; during multiplication bacteriophage increases in concentration; only after a certain time elapses does lysis or dissolution make its appearance; following rapid dissolving or lytic action, bacteriophage ceases to increase in amount; during the rapid multiplication of bacteria no definite demarcations are formed between the bacterial cells, as is ordinarily the case, but the elements remain in unseparated chains; the bacterial elements swell. During this process the bacteria take the stain less intensely and regularly and show a granular disintegration; the bacteria finally disappear. (According to very interesting cinematographic records taken by Bronfenbrenner, it was shown that this disappearance takes less than two seconds.)

Summarizing briefly, the explanation of the bacteriophage phenomenon, consisting of the dissolution of bacteria by ultramicroscopic agents, is as follows: When bacteriophage, which is a poisonous product of the bacterial life-process, attacks normal bacteria, it causes a rapid multiplication of the latter. Further, it enhances the metabolism of the bacteria, causing the intracellular enzymes, which accelerate chemical changes in the body, to become more active. Some of the intracellular material is digested by the heightened enzymic activity. This causes an increase in the osmotic pressure of the bacterial cell, whereupon the cell imbibes water and bursts. The bursting and disappearance of the bacterial cell, however, do not follow immediately upon its contact with bacteriophage. In fact, the time elapsed between the production of bacteriophage during the stage of rapid multiplication of bacteria and the bursting of the bacterial cells is approximately four hours.

Investigators have attempted to produce bacteriophage artificially or spontaneously from normal bacteria, but their results have remained unconvincing. The metabolic processes of bacteria are complex, and accurate knowledge concerning them is still limited. The phenomenon called "bacteriophage" has proved baffling in the extreme.

The microscope tells us what bacteria are; clinical medicine deals with the disease-producing activities of bacteria; but what lies beyond the microscope remains for the research laboratory to reveal.

Chapter XXI

ANTITOXIN, VACCINE, WASSERMANN TEST, AND HYPERSENSITIVITY

I. ANTITOXIN

An antitoxin or vaccine is something more than a "shot in the arm." To be sure, the injection is a protection against infectious disease, but its why and wherefore is no simple tale. Immunologic tomes are written upon the subject of vaccines and antitoxins, but none are easily epitomized. To plunge into the heart of the matter at once, it may be said that in the course of bacterial growth certain poisons, called "toxins," may be produced. Toxins may be secreted and retained within the bacterial cell, as in the tubercle bacillus; or they may be excreted, as in the diphtheria bacillus. The former are known as intracellular, or endotoxins; the latter, extracellular, or exotoxins. Toxins are neutralized in the blood-stream by antitoxins. To comprehend how this is accomplished it is necessary to have some better understanding of toxins.

Toxins are poisons elaborated during bacterial growth. They are so potent that even minute amounts are deadly. Jordan gives the following interesting table in support of the statement that "the potency of the bacterial toxins is extraordinary, and far surpasses that of any other known poison":

Minimal fatal dose of atropin for adult man	130 mg.[1]
" " " " strychnine for adult man	30 to 40 mg.
" " " " cholera venom for " "	4.375 mg.
" " " " tetanus toxin " " "	0.230 mg.

The exact chemical nature of toxins remains unknown, but we do know that they belong to the complex proteins and are easily destroyed by heat or chemicals. Each toxin has its own specific action — that is, it produces certain definite and constant

[1] A milligram (mg.) is one-thousandth of a gram. There are four hundred and fifty-four grams in a pound.

symptoms when introduced into the animal or human body. A true toxin necessarily calls forth the production of antitoxin. Extracellular or exotoxins, such as are produced by the diphtheria and tetanus bacilli, are soluble — that is, they pass out of the bacterial cell into the surrounding medium. Intracellular or endotoxins are, on the other hand, retained within the bacterial cell and are probably liberated only upon the death and disintegration of the cell. Endotoxins are generally regarded as split products of bacterial proteins and do not give rise to antitoxins.

FIGURE 90

Ehrlich's conception of toxin and antitoxin; the horseshoe-like structures being toxin molecules. The oval droplets which fit into them and neutralize them are antitoxin bodies. (After Park, Williams, and Krumwiede.)

An antitoxin is a counter substance (composed of what are called "antibodies") which is formed in an animal as the result of stimulation from a particular toxin. Antitoxins are simpler and more stable than toxins, but their nature also remains undetermined. They are classed with the higher proteins. Antitoxins are strictly specific; that is, they neutralize only the particular toxin which stimulated them into being. Thus diphtheria antitoxin neutralizes diphtheria toxin, but not tetanus toxin.

Ehrlich gave a very brilliant and graphic account of his theory of the action of toxin and antitoxin. (See fig. 90.) It is described as a "lock and key" theory. The toxin molecules floating in the blood unite with the antibodies, this chemical union preventing the toxin molecule from attaching itself to the blood-cell, which it would otherwise poison. Many salient details are here purposely omitted in an effort to reduce the matter to its simplest terms, which are admittedly complex.

The production of diphtheria antitoxin may well serve as a representative illustration. In order to produce antitoxin it is first necessary to have a powerful toxin. The latter may be obtained by growing the diphtheria bacillus artificially, and filtering off and concentrating the toxin which the bacilli excrete. Then the toxin is injected in increasingly larger amounts into healthy young horses. Obviously, the toxin injected stimulates the production of antibodies. The animal is bled, the blood clots, and the liquid portion or serum is utilized. (A disinfectant

is usually added to the serum to prevent microbial contamination.)

This specific serum is now known as "antitoxin." It is standardized by determining how many units will neutralize a given amount of toxin. The antitoxin may be diluted or concentrated as desired. The physician is then able to regulate the number of units of antitoxin administered. About five hundred units are used to protect against diphtheria infection; about three thousand to twenty thousand units are employed in the treatment of a patient with diphtheria. The immunity thus conferred is known as "passive immunity," since the antibodies which neutralize the toxins formed by the diphtheria bacilli are introduced into the body from without. The body merely serves as a test-tube in which neutralization of the toxin takes place.

2. VACCINE

Active immunity is conferred upon an individual by stimulating him to produce his own supply of antibodies. This is accomplished by the introduction of killed or attenuated cultures of the organism in question. Thus typhoid vaccine is prepared by washing a young growth of typhoid bacilli off a solid medium by means of sterile saline solution. The bacilli are then killed by subjecting them to a temperature of 128°F. for one hour and adding some disinfectant for good measure. Three to four doses, ranging from five hundred million to a billion dead bacilli, are injected into an individual at about weekly intervals. It must seem very surprising that dead bacilli are capable of exerting an influence on bodily reactions. Nevertheless, we must remember that bacilli, dead or alive, have a very definite chemical composition and that these components cause a reaction in the human body, especially as concerns the production of antibodies. Protection against infection from typhoid fever is thus obtained by vaccination and it is believed that such immunity lasts for about two years.[1]

[1] At this point may be mentioned Besredka's theory of local immunization. Its important feature is that immunity may be established in certain bodily structures — as, for example, the skin (for anthrax infections), or the intestinal lining (for typhoid fever) — rather than depending upon a circulation of antibodies in the bloodstream.

3. WASSERMANN TEST

The Wassermann reaction is a very complicated phenomenon. The Wassermann test for syphilis is one of the most important laboratory aids in the clinical diagnosis of syphilis. It depends on the so-called Bordet-Gengou phenomenon of complement fixation, which is difficult to describe in non-technical language. For the reader who may be interested, however, the following summary is presented.

Let us focus our attention upon complement. It is a normal constituent of red blood cells. Complement is a binder. It has the capacity of binding antigen to antibody. Antigen is a substance which upon injection stimulates the production of antibodies — which are specific substances capable of uniting with antigen. When exactly the right amount of complement is added to a mixture of antigen and antibody, the complement is "fixed" — that is, it binds the antigen to the antibody. If complement is not "fixed," that means the antibody and the antigen are not related. In that event, free complement may, of course, unite further related antigens and antibody which may be added.

In practice, therefore, an animal is immunized against a certain microbe or cells by the injection of gradually increasing doses. Blood is drawn from the immune animal, and the serum heated to 133°F. This inactivates it or destroys its complement, which is a substance capable of destroying the invading microbe or cells through the intermediary agency of amboceptor. Amboceptor is not destroyed at 133°F., as is complement. But amboceptor which attaches itself to the invading microbe or cells cannot kill them alone. Amboceptor and complement are like Siamese twins. The cells to which amboceptors are attached are termed "sensitized." In order to disintegrate them fresh complement must be added to the sensitized cells. The phenomenon of complement fixation is applied to syphilis.

An analogy has been drawn by Rosenau between the Wassermann test and the geometric problem: knowing two sides and an angle of a triangle, determine the other side and angles. Syphilitic antibody is unknown. It is or is not contained in the patient's serum, of which a small amount is used. Before the suspected

serum is used, it is heated to destroy *its* complement. The unknown is (1) the patient's serum. The known substances are: (2) the antigen — which, like a toxin, is any substance capable of producing antibodies upon injection. Alcoholic extracts of known syphilitic organs, beef heart, spleen, etc., serve as antigens. (3) Free complement — which is a constituent of normal or immune serums capable of dissolving red blood cells, when acting in conjunction with amboceptor. It is obtained from the serum of guinea-pig's blood. The patient's serum, antigen, and complement are mixed in a tube and heated to 100°F. for about forty minutes. Syphilitic antibody present in the patient's serum is fixed to the antigen by complement. If no syphilitic antibody is present, some free complement remains. (4) Blood corpuscles from a sheep — these are washed with sterile saline solution. Complement is of course present. (5) Hæmolytic serum — this is prepared by immunizing a rabbit with injections of increasing doses of these sheep cells. The serum from this rabbit's blood is inactivated by heating at 131°F. for one half-hour. The amboceptor remains intact, but the complement is destroyed. Standardization of amboceptor and complement is highly important, since suitable amounts of each must be employed.

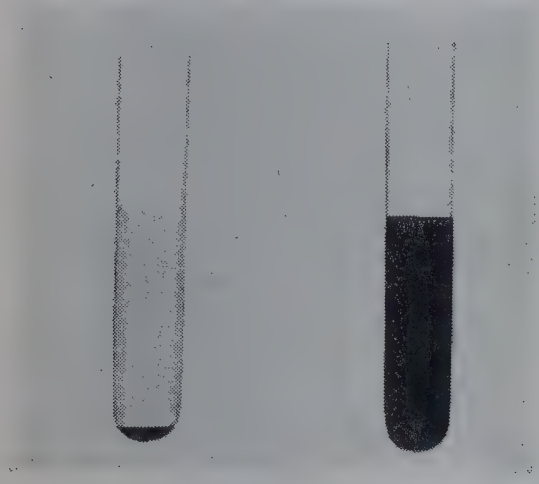


FIGURE 91

The Wassermann test. Positive, showing precipitation of blood cells, at the left. Negative, showing blood cells dissolved, at the right.

Now the five components — patient's serum, antigen, complement, sheep cells, and immune rabbit serum are mixed and heated to body temperature (98.6°F.). If the patient's serum contains syphilitic antibody, the sheep's red blood cells do not dissolve, but fall to the bottom of the tube, because complement has already been fixed by syphilitic antibody and cannot fix the sheep-cell antigen to the antibody formed in the patient's serum. This is known as a "positive reaction," and the patient has syphilis. The intensity of the positive reaction is arbitrarily termed "one plus" (+), "two plus" (++), "three plus" (+++) and "four plus" (++++). If the red blood cells

are dissolved, however, then complement has not been fixed by syphilitic antibody, but by the sheep's blood-cells and antibodies. The reaction is therefore negative and the patient does not have syphilis. In carrying out the Wassermann test, controls should be run on normal serum and known syphilitic serum. (See fig. 91.)

There are many modifications of the Wassermann test and other reactions for syphilis which need not be here described. Direct precipitation tests are now being favoured, particularly that of Kahn.

4. HYPERSENSITIVITY (HAY-FEVER, ETC.)

The Wassermann reaction is a serious matter, but no such gravity attends the practical and interesting phenomenon of *hypersensitivity*, of which hay-fever is the best example. The professional jokesmith would be hard put to it if he could not pounce on the perennial hay-fever victim. The latter cuts a distressing figure. He tastes not, neither can he smell. His thickened speech is the columnists' delight. Hypersensitivity indeed! One might believe the term was used to describe the victim's emotional reaction rather than the fact that he is peculiarly susceptible to some otherwise innocuous pollen or foodstuff. What is one man's meat is another man's poison. Egg white, strawberries, fish, nuts, etc., may serve to bring on skin eruptions or inflammation of various kinds. Horse dander, or other animal emanations, cat's fur, chicken or goose feathers stuffed into pillows, may all serve as unnoticeable agents inciting inflammation of the mucous membranes of the respiratory tract.

Older people suffer less frequently than young persons, and there are fewer male than female victims. Heredity plays an important rôle in the transmission of hypersensitivity. The symptoms give no index of the cause, and several methods have been devised for tracking down the inciting agent. The most commonly used is that of a series of skin scratches to which various suspected pollens or other proteins are applied. Hypersensitivity to a particular pollen is indicated by the formation of a red wheal on the injected arm. The patient may then avoid

the offending protein — for it is always a protein — or, if he cannot avoid it, he may become desensitized. This is accomplished by injecting at first minute quantities and later larger amounts of the protein substance at fault. Such treatment should be started from six to eight weeks before the anticipated attack. Hay-fever victims are so constituted that they can foretell not only the month, but the day, perhaps even the hour, when the first sneeze inaugurates their open season. Immunity obtained by desensitization is unhappily not lasting.

Hypersensitivity under certain rare conditions may prove fatal. This is known as anaphylactic shock. Cases have been reported in which patients suffering from asthma died following an injection of the protein to which they were hypersensitive. Thus Boughton injected a minute amount of horse serum into a patient with "horse asthma" with fatal results. Serum sickness characterized by a rash or swelling sometimes occurs after the injection of antitoxin which contains horse serum, but there really need be no concern here of anaphylactic shock.

The phenomenon of hypersensitivity is a complex one, about which we know little. In some respects it resembles the antigen-antibody reactions to which reference has already been made. Hypersensitivity may well have a bearing upon the protection of human beings against infectious diseases. Bacteria are protein in nature. The introduction of foreign bacterial proteins into the human body may cause certain undesirable responses, which are not altogether due to toxins formed by bacteria. It is only recently that the study of hypersensitivity has been placed upon a scientific experimental basis. It is now recognized as an interesting branch of the profound subject of immunity.

Chapter XXII

DISEASE-PRODUCING MOULDS

I. THE HIGHER BACTERIA

In the foregoing account of disease-producing bacteria we have run the gamut from those which are ultramicroscopic in size to the comparatively large spirochætes. There are other organisms still to be considered which resemble moulds or fungi so closely that there is great difficulty in classifying them with the bacteria described. For want of a better name they are known as the "higher bacteria" or "trichomycetes." Their growth is characterized by long threads, usually branched. To be sure, branching forms are to be encountered in the bacteria already discussed, notably along the tubercle, diphtheria, and glanders bacilli; but in the higher bacteria extensive branching is the rule.[1] (See fig. 92.)

Figure 92

Higher bacteria. Actinomyces at the left; Cladothrix at the right.

The most important of the higher bacteria are the Actinomyces. They produce the disease called "actinomycosis," which is characterized by the formation of pus and a destruction of local tissue, which resembles cancer. The disease occurs less frequently in the United States and England than in Germany. Osler says that it is "nearly three times as common in men as in women." Cattle

[1] As always, however, there must be an exception to spite the generalization. In this case it is the Leptothrix group of bacteria, which are often found in inflammations of the mouth and throat and belong with the higher bacteria, although they form simple threads without branching. It is extremely difficult to cultivate this group artificially, and since no member is directly implicated as the specific cause of inflammatory conditions, it need not detain us.

are also affected, the disease going by the descriptive name of "big jaw." It also occurs in sheep, horses, pigs, dogs, and cats.

Israel discovered the human parasite in 1878. In pus it appears as a small greyish-yellow granule, which upon closer microscopic examination proves to be a network of branching threads, some with characteristic club-shaped ends, and cocci. It can be cultivated artificially.

Diseases similar to actinomycosis are caused by other higher bacteria called "Nocardia." They may cause abscesses in the lungs, brain, skin, etc., as well as general blood-poisoning. Madura foot, or mycetoma, is a closely allied disease, which occurs chiefly in India. It is characterized by local inflammation, nodular growths, and the development of numerous abscesses. Generally the sole of the foot swells and the foot becomes tremendously enlarged. The disease is caused by an organism closely resembling the actinomyces. The treatment for all of the diseases caused by the higher bacteria is chiefly surgical.

2. YEASTS

Yeasts (saccharomyces) have been defined as moulds which multiply by budding. Moulds, or fungi, it will be recalled, are plants which have neither stems, roots, nor leaves and are devoid of chlorophyll. While yeasts are best known for their

FIGURE 93

Yeast cells. With adhering daughter cells at the left; with spores at the right. (After Conn and Conn.)

power to ferment sugar, certain species of yeasts must be reckoned with in the causation of disease. An adult yeast cell is usually round or oval and its diameter is somewhat greater than the length of a spirochæte. (See fig. 93.)

Blastomycosis is one of the most common diseases due to yeast infection. It takes two principal forms: infection of the skin, and infection of the blood-stream. Frequently the lungs are

affected. Yeasts may be cultivated from the pus and when grown on solid media have the appearance of *Staphylococcus albus:* white glistening spots. Different yeasts grow differently; some remain smooth, others become wrinkled or form white threads. They show a marked preference for an abundant oxygen-supply. All yeasts grow brown with age.

Thrush is a disease of the mouth or throat which occurs chiefly in children and is caused by a yeast — *Monilia albicans.* (See fig. 94.) The disease begins with white pearly spots on the tongue, which increase in size until they become confluent. Creamy patches spread to the tonsils, throat, lips, and cheeks.

FIGURE 94

Monilia albicans, the cause of thrush. Right, greatly magnified. (After Marshall.)

The disease does not occur in normal and healthy mouths. Improper diet and uncleanliness of the mouth, of feeding bottles, or of spoons is usually responsible for thrush in children. To quote Osler, "Robust well-nourished children are sometimes affected, but it is usually met with in enfeebled, emaciated infants with digestive or intestinal troubles. In such cases the disease may persist for months. . . . It is not confined to children, but is met with in adults in the final stages of fever, in chronic tuberculosis, diabetes and in cachectic states."

Sprue is another important disease believed to be caused by a yeast, *Monilia psilosis.* It occurs chiefly in the tropics and is characterized by "a peculiar, inflamed, superficially ulcerated, exceedingly sensitive condition of the tongue and mouth; great wasting and anæmia; pale, copious and often loose, frequent, and frothy fermentating stools; very generally by more or less

diarrhœa; and also by a marked tendency to relapse" (Manson). There is considerable debate as to whether or not *Monilia psilosis* is the primary cause of sprue or whether its presence is incidental in this disease.

Yeast-like parasites are responsible for a number of skin and other diseases in addition to those already mentioned. Animals, too, suffer from yeasts. Horses, for example, have yeast infections which are easily mistaken for glanders.

3. MOULDS

Have you ever noticed the greenish patches on a decaying lemon or orange — or on shoes or trunks which have been in a damp place? You say that the object is mouldy, which is true, for moulds are actually growing upon it.

FIGURE 95

Moulds. Above, mycelial threads with fruiting bodies holding spores. Below, different kinds of fruiting bodies holding spores. (After Conn and Conn.)

Moulds, or fungi, are made up of cylindrical cells, microscopic in size, which form long threads, visible in masses to the naked eye. (See fig. 95.) Many of these threads end in rounded bodies called "spores," which correspond to the seeds of plants. Unlike bacteria and yeasts, true moulds may reproduce asexually, by extension of threads, or sexually, by means of true spores, which represent the union of male and female cells and whose sole function is reproduction. Some spores formed by moulds, it should be mentioned, are vegetative — that is, concerned more with growth than reproduction. Spores and the structures which support them have characteristic colours, some black, some green, etc. Thus mouldy bread is usually black, because the mould which is ordinarily found on bread produces black spores; on oranges mould growth is generally green, owing to the presence of a different species. Classification of moulds is extremely difficult, so that it need only be said that the differ-

entiation of moulds rests largely on the characteristic formation of spores or threads, which must be subjected to careful microscopic examination.

Moulds cause disease in man, usually of the skin. Sporotrichosis is an affection of the skin and internal organs closely resembling syphilis. It is comparatively rare in the eastern United States, but occurs not infrequently in the South-west, as well as in France and Switzerland. Schenck first described the disease in this country in 1898. Horses, dogs, and rats are affected as well as man. The diseases caused by certain species of moulds belong to the genus *Sporotrichum*. They may be easily cultivated in the laboratory.

There are a number of diseases of the ringworm group, known as "dermatomycoses," caused by other moulds, which are usually restricted to the outer layers of skin. Favus, for example, is such a disease, characterized, as Zinsser says, by "the formation at the mouths of the hair follicles of small, yellow, cup-shaped crusts known as *Scutula*." The most widely known disease of this large group is ringworm, or tinea, which is the contagious scalp disease of children. Epidemics of ringworm are the bane of children's schools and institutions. The name of the disease, "ringworm," resembles "tapeworm" so much that it may connote some form of animal infestation. But the circular bare patches which characterize this disease are caused by mould growth, moulds being the lowest form of plant-life. Domestic animals are similarly attacked, and often children become infected by contact with diseased animals.

There are hosts of moulds causing different kinds of ringworm disease; thirty species are listed for one genus alone, *Trichophyton*. Some attack other parts of the body, such as the groin, while others are limited to the hair and nails.

Ordinarily one would not suppose that bacteriology comprises more than the study of bacteria; it must, however, include yeasts and moulds, which are important not only in the causation of disease, but also in agriculture and industry, as will be shown in a later chapter.

Chapter XXIII

DISEASE-PRODUCING PROTOZOA (MALARIA, ETC.)

Having considered the lowest forms of plant-life as factors in the causation of disease, we now come to the lowest form of animal life, the protozoa. The protozoa are single cells, microscopic in size, but usually larger and much more complex in structure and life cycle than bacteria. (See fig. 96.) The principal point of difference between protozoa and bacteria is that the

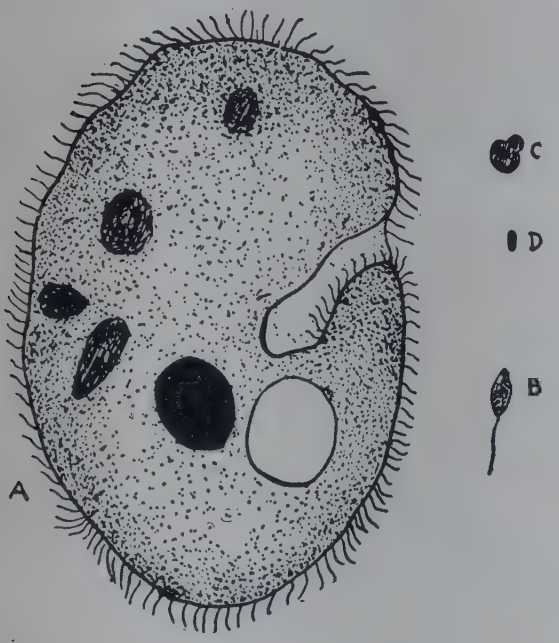


Figure 96

Relative size of protozoa, yeasts, and bacteria. A, large protozoon; B, small protozoon; C, yeast; D, bacterium. (After Conn and Conn.)

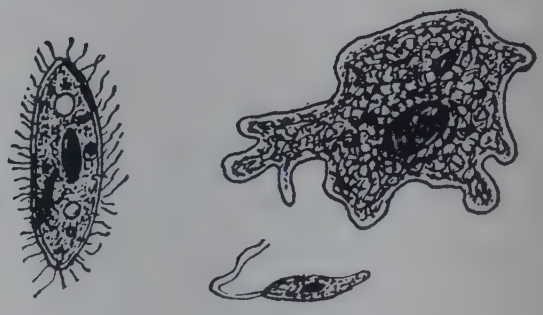


Figure 97

Different kinds of protozoa. (After Conn and Conn.)

former have a nucleus, which stains differently from the remainder of the cell constituents, while the bacterial cell stains more or less homogeneously with the ordinary technic. The nucleus of the protozoa stains red and the body or protoplasm stains blue. All protozoa are motile, some possessing flagella or cilia, others moving by means of pseudopodia, "false feet." (See fig. 97.) Reproduction, as with moulds, may be asexual — that is, by division — or sexual. (See fig. 98.)

I. MALARIA

Malaria has come down through the ages and is distributed throughout the world.

Sir Ronald Ross, who was knighted in recognition of his important contributions to the subject, writes: "Malarial Fever is, perhaps, the most important of human diseases. Though it is not often directly fatal, its wide prevalence in almost all warm climates produces in the aggregate an enormous amount of sickness and mortality. In India alone, it has been officially estimated to cause a mean annual death-rate of 5 per thousand; that is, to kill every year, on the average, 1,130,000 persons — a population equal to that of a great city. The total amount of sickness due to it is incalculable, but may be put by a rough estimate at between a quarter and a half the total sickness in many tropical countries. Often all the children and most of the adults are infected by it. Very malarious places cannot be prosperous: the healthy shun them, those who remain are too sickly for hard work, and such localities often end by being deserted by all save a few miserable inhabitants. Malaria is the great enemy of the explorer, the missionary, the planter, the merchant, the soldier, the farmer, the administrator, the villager, and the poor, and has, I believe, modified the world's history by tending to render the whole of the tropics comparatively unsuitable for the full development of civilization. It is essentially a political disease — one which affects the welfare of whole countries; and the prevention of it should therefore be an important branch of public administration."

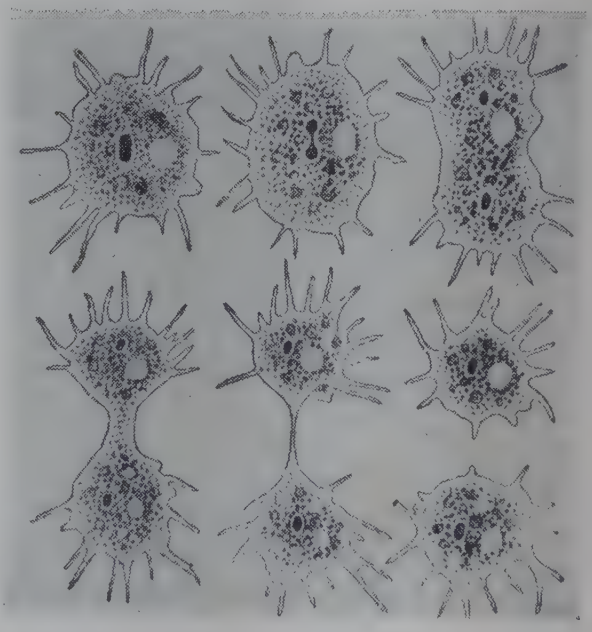


FIGURE 98

Stages in the reproductive division of an amœba, showing elongation and then separation. (After Marshall.)

Malaria has been known since antiquity, under many names, such as "chills and fever," "Roman fever," "Chagres fever,"

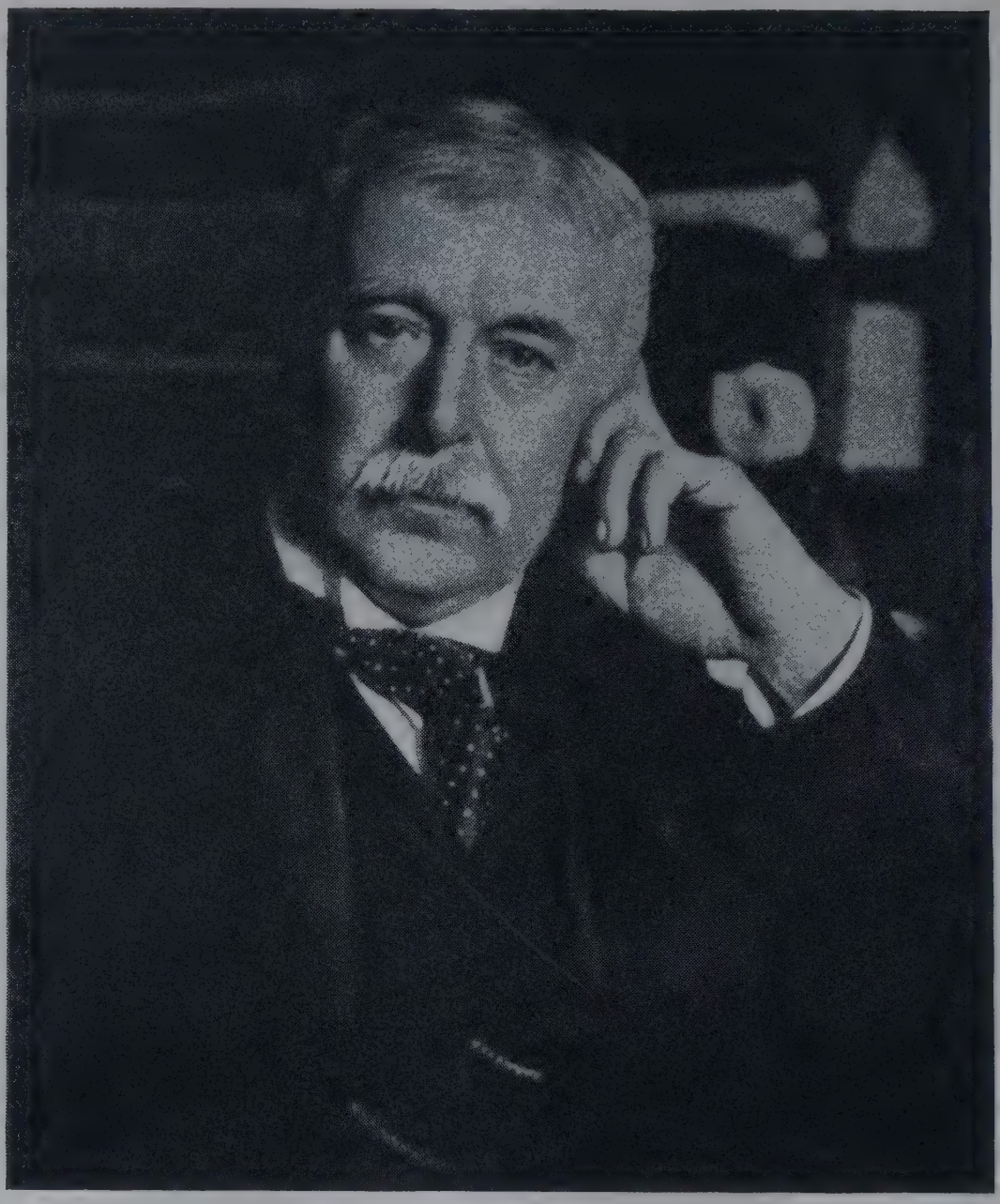


FIGURE 99
Patrick Manson. (After Ross.)

etc. But it was not until 1880 that its cause was discovered. Laveran, a French military surgeon stationed in Algiers, first identified under the microscope certain parasites in the blood which he considered responsible for the disease. But how does the malarial parasite enter the blood-stream? And why is there more malaria in swampy regions? The answer to these questions was indicated by Patrick Manson (see fig. 99), who believed that malaria was transmitted by the bite of some blood-sucking insect, in all likelihood the mosquito. Ross, of the British Indian Medical Service (see fig. 100), following this lead, described in 1897 the life cycle of the parasite in what he termed

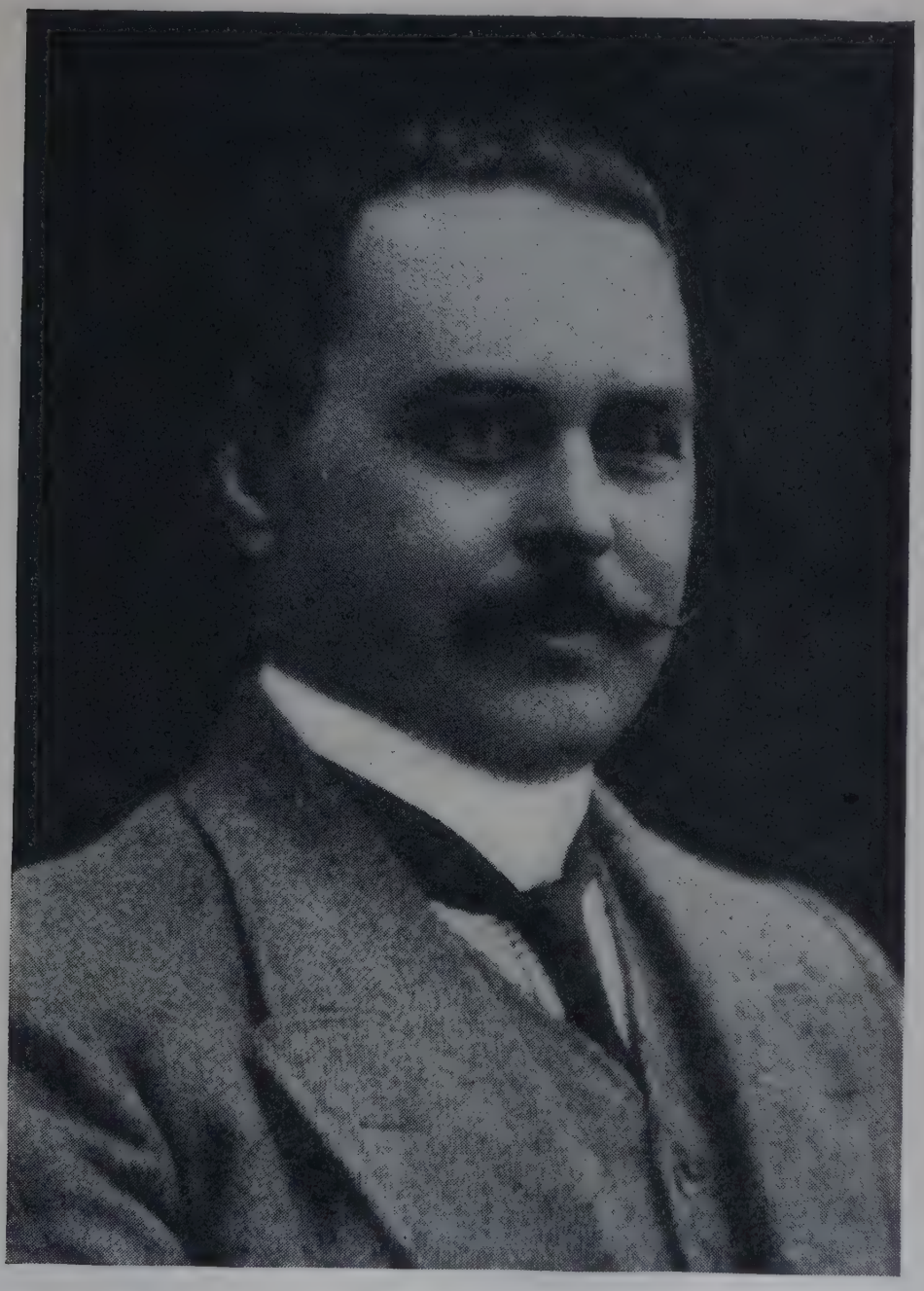


FIGURE 100

Ross. (*After Kelly.*)

a "dapple-winged" mosquito, now called "*Anopheles.*" Independently of Ross, in 1898, three Italians, Bastianelli, Bignami, and Grassi, also described the complete life cycle of malaria in the *Anopheles.*

In order to prove that the mosquito transmits malaria Manson outlined an experiment which was carried out by Sambon and Low in the Roman Campagna. By the simple expedient of screening dwellings, which kept out mosquitos, they established that it was possible to live in a malarial locality without contracting the disease. The final demonstration of the actual

transmission of malaria by mosquitos was still to come. Manson in London imported from Rome *Anopheles* mosquitos known to harbour malarial parasites and allowed them to bite his son, P. T. Manson, and G. Warren, neither of whom had ever contracted malaria. Manson wrote the details of this memorable experiment to Sambon as follows:

"You know Burnie [his son] was bitten by the Roman mosquitos about the beginning of July, again at the end of August, and again about ten days ago. He kept quite well until last Thursday, the 13th. That morning he got up feeling cheap; temperature 99. During the day his temperature rose to 102, but as blood examination revealed no parasites, I did not permit myself even to hope. Next day the same — continued fever of 100 to 101.8 and febrile feelings; still no parasites. At 2 p.m. he was so well that I went down to Chalfont. I was seedy, gouty and influenzal. On Saturday evening, as we sat down to dinner, I received a telegram from Edie saying that Burnie had high fever. When I got home on Monday morning, Burnie was still sitting up feeling well though played out, and he told me that on Saturday night temperature after chills had gone up to 104 and that he had delirium. The fever ended in profuse drenching sweat. Sunday forenoon he was quite well, but the same fever recurred on Sunday afternoon. When I examined his blood, in a few minutes I found a tertian parasite — half grown, some pigmented leucocytes. It was a case of Eureka indeed. Many blood examinations only confirmed the first finding. Monday — yesterday — afternoon again fever to 103. I got six men to verify the observation, telegraphed to you and others, and when the temperature began to fall about 9 p.m., gave him ten grains of quinine. He has been taking quinine since; and though there are still a few parasites in his blood, including gametes, he is now quite well and examining his own blood. This, of course, is immense, and together with your success proves our points up to the hilt."

The life cycle of the malarial parasite is complex — in fact, it has two life cycles, one in the mosquito and one in man. Let us first consider the life cycle in the mosquito. Male and female malarial cells enter the stomach of the mosquito when it sucks up blood from an infected person. They fuse and the fertilized

cell develops in the stomach lining of the mosquito, finally forming a sac containing sporozoites. The sac ruptures and the sporozoites invade the blood-stream of the mosquito, many of them being carried to the salivary glands. When this mosquito bites a person, the sporozoites harboured in the salivary glands are introduced into the human host.

The sporozoites penetrate the red blood cells and begin to grow in them. At first they present a "signet-ring" appearance.

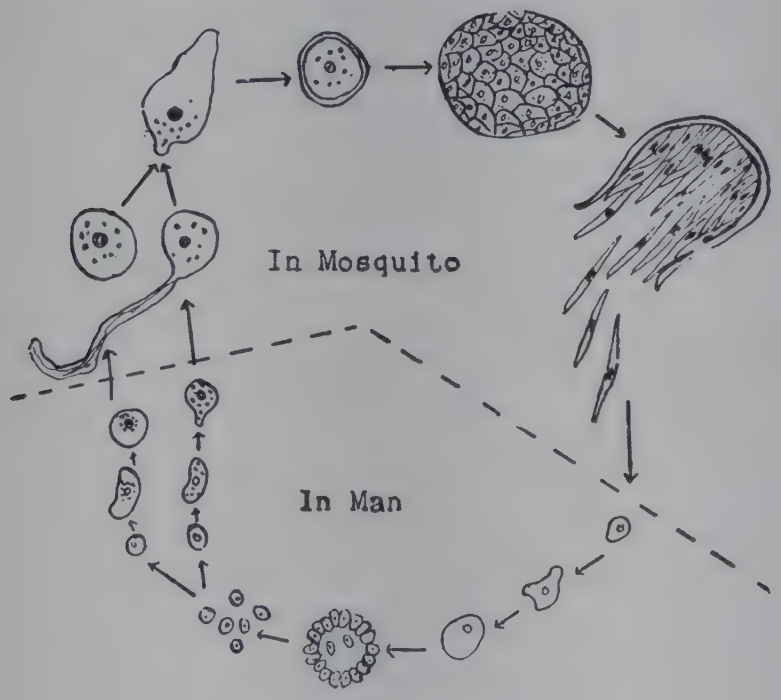


FIGURE 101

Life cycle of the malarial parasite in the mosquito and in man. In the mosquito (from left to right) are male and female cells which fuse, forming a sac, containing sporozoites, which ruptures. In man (from right to left) the parasite develops, finally segmenting to release merozoites, or producing male and female cells. (After Conn and Conn.)

Then they develop into large irregular amœboid forms at the expense of the red blood cells which they inhabit. When fully developed, the parasite segments and the merozoites which have been formed escape into the blood-stream of the human host to enter other red blood cells and complete the asexual cycle of reproduction. The sexual cycle in the human host is observed when, instead of segmentation forms, other sexual forms, male and female, are developed. When the mosquito sucks up blood containing these sexual forms, the life cycle described in the mosquito is begun. (See fig. 101.)

Thus man infects the mosquito and the compliment is returned. Whereas the mosquito does not suffer by playing host to the malarial parasite, man develops certain characteristic symptoms. Chills and fever are the most striking evidences of malaria. During the chill, which may be so severe that the shaking of the body may even cause the bed to shake, headache, nausea, and vomiting frequently occur. Following this cold stage is the hot stage, when the fever becomes intense and the patient parched with thirst. Profuse sweating ensues and the fever breaks. Anæmia and an enlarged spleen are usually to be observed.

There are several types of malarial fever: tertian (intermittent fever, with the peak every forty-eight hours), and double tertian or quotidian (with the peak every twenty-four hours); quartan (intermittent fever with the peak every fourth day); and æstivo-autumnal (irregular or continued fever), occurring in late summer or autumn. The last is the most dangerous form of malarial fever from the standpoint of mortality. Liver and kidney complications as well as pneumonia are frequently encountered in malarial fevers. Black-water fever follows malaria in certain districts. Relapses or recurrences are very common.

The treatment of malaria is familiar and consists in the prompt administration of quinine, which is a specific remedy against this infection. Prevention of malaria has made rapid and gratifying progress and depends primarily upon: the eradication and destruction of mosquitos by proper drainage and filling in of swampy lands, and the use of oil on breeding-places; screening of houses against invasion by mosquitos; and adequate treatment of infected individuals, to preclude their carrying the disease.

The therapeutic value of malaria in the treatment of general paralysis has been discussed in connexion with syphilitic disease in chapter XVI.

2. AFRICAN SLEEPING-SICKNESS

African or true sleeping-sickness should never be confused with what is now popularly called "sleeping-sickness" (*encephalitis lethargica*). The cause of the latter is still obscure, the

symptoms variable, and the treatment doubtful. On the other hand, it is firmly established that African sleeping-sickness is caused by protozoa called "trypanosomes" and that the disease pursues a characteristic course. In the first stage, there is "fever with rapid pulse, dulling of the mind, and loss in weight; secondly, the stage of tremors in which the gait becomes shuffling, the speech slow, and there are tremors of the tongue and of the hands, and feet; lastly, a stage in which the patient becomes lethargic with low temperature and presents the typical picture of the dreaded sleeping sickness" (Osler).

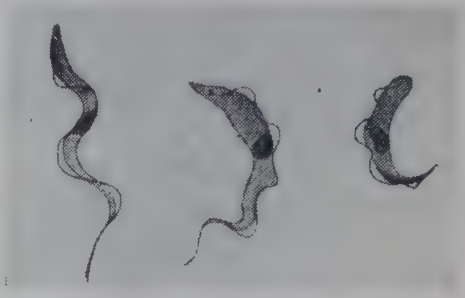


FIGURE 102

The cause of African sleeping-sickness, Trypanosoma gambiense. (After Doflein from Minchin in Marshall.)

The disease was well known in West African natives and in slaves imported from western Africa. It has been estimated that a hundred thousand Negroes died of African sleeping-sickness in Uganda during the three years that this site was first opened up. Europeans as well as Negroes have been infected.

The specific protozoon causing the disease is *Trypanosoma gambiense*, a spindle-shaped organism, much longer and wider than a spirochæte. It has a long, whip-like flagellum. (See fig. 102.) Forde first found the parasite in the blood of a patient who died of the disease. A year later, in 1902, Dutton described it accurately as a trypanosome, and Castellani in 1903 indicated its causal relationship by finding it in the spinal fluid of natives suffering from the disease in Uganda.

FIGURE 103

Tsetse fly, which spreads African sleeping-sickness. Above, before a meal; below, after a meal of blood. (After Conn and Conn.)

Like malaria, African sleeping-sickness is a protozoon disease, transmitted by an insect, this time the tsetse fly. (See fig. 103.) The disease is effectively treated by arsenicals, notably atoxyl and "Bayer 205." It is interesting in this connexion to remember that Ehrlich's great discovery of "606" developed from his work with trypanosomes and his desire to find a chemical which would kill them. The brilliant results obtained in killing trypanosomes with "606"

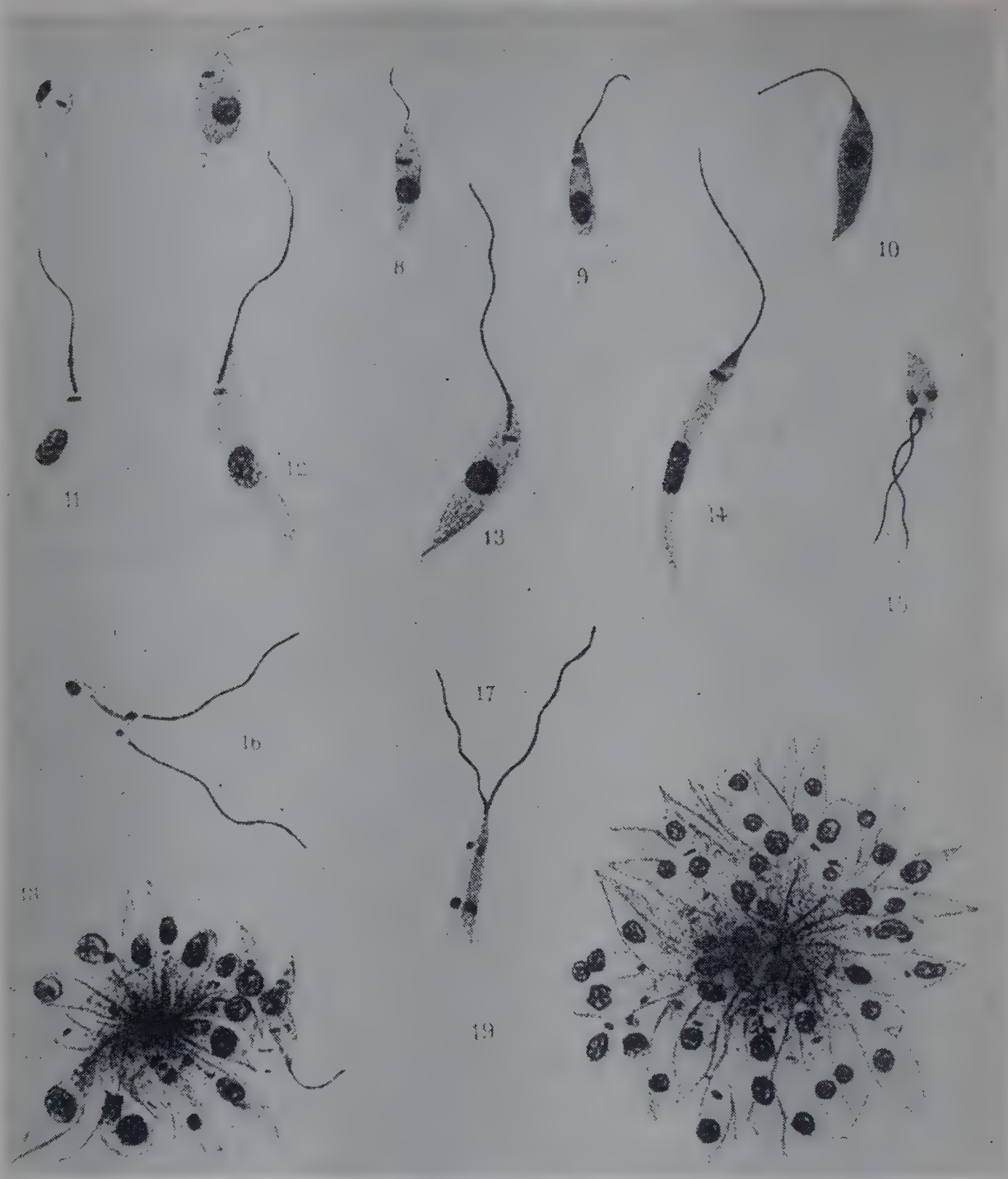


FIGURE 104

Leishmanias. (*After Park, Williams, and Krumwiede.*)

were then surpassed by Ehrlich in the treatment of syphilis. Prevention of African sleeping-sickness depends upon the eradication of the tsetse fly, which bites only by day. Since it is impracticable to remove the tropical growth of infected regions and thereby eradicate the tsetse fly, travelling is best done at night.

Another type of African sleeping-sickness, somewhat more acute, and yielding less readily to treatment, is caused by *Try-*

panosoma rhodesiense. A similar parasite is *Trypanosoma cruzi Chagas*, which causes fever, swelling of the thyroid gland, nervous symptoms, and often death.

In discussing animal diseases some mention of trypanosomes has already been made. To enumerate the principal ones briefly: *Trypanosoma rotatorium* — the first trypanosome to be described — occurs in frogs, salamanders, reptiles, and fishes; *Trypanosoma lewisi* does not produce disease and is found in grey rats; *Trypanosoma evansi* causes surra, a febrile disease of horses, mules, camels, elephants, buffalo, and dogs; *Trypanosoma brucei*, transmitted by the tsetse fly, causes a weakening disease called "nagana," of economic importance in domestic animals (see figs. 101, 102); *Trypanosoma vivax* causes a disease called "souma" in cattle, sheep, and goats; *Babesia* (*Piroplasma*) *bigeminum* causes the serious disease called "Texas fever" in cattle, transmitted by the tick; *Trypanosoma hippicum* causes a similar disease of horses and mules; *Trypanosoma equiperdum* causes dourine, a sexually transmitted disease, in horses and donkeys; *Trypanosoma avium* is found in birds, but does not produce disease.

Closely related to the trypanosomes, but very much smaller in size, are the *Leishmanias*, responsible for various tropical diseases. (See fig. 104.) Chief among these is kala-azar, characterized by intermittent fever of long duration, emaciation, enlargement of the spleen and liver, etc., and an extremely high mortality (eighty to ninety per cent in untreated cases). *Leishmania donovani* is the protozoon causing this disease. It is an elliptical micro-organism about the size of an extremely large coccus. The disease is effectively treated by sodium antimony tartrate. *Leishmania tropica* is a similar protozoon causing the skin disease variously known as "Delhi boil," "Aleppo boil," "oriental sore," and "tropical ulcer." *Leishmania braziliensis* also causes a disfiguring ulcerative disease of the skin.

3. AMŒBÆ

The most familiar disease caused by those protozoa called "amœbæ" is amœbic dysentery. This disease, known to antiquity, is common in Egypt, India, the southern United States,

and the tropics. The disease, which is usually chronic, is characterized by severe pains, diarrhœa, mucus and blood in the stools, emaciation, ulcers in the intestinal tract, and often abscess of the liver. Compared with dysentery caused by bacilli, as described on page 126, amœbic dysentery is more difficult to detect because for a long time the victim may be fairly comfortable and unaware of the gravity of his condition.

Endamœba histolytica is the protozoon which causes amœbic dysentery. It is a large, rounded micro-organism, with a diameter greater than that of most spirochætes. (See fig. 105.) It moves by changing its shape — that is, by means of pseudopodia.

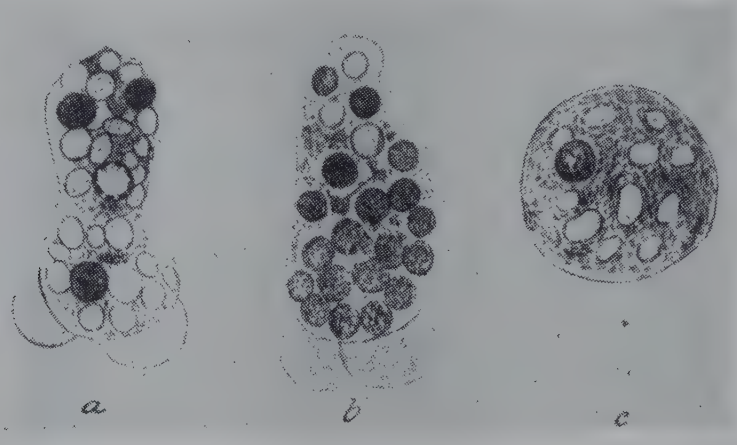


FIGURE 105

Endamœba histolytica, showing the ingestion of red blood corpuscles, at the left and centre. (After Jordan.)

Reproduction is effected by division. Amœbæ are found with much more frequency in the intestinal tract than was heretofore conjectured. In tropical countries it has been estimated that fifty per cent of the population harbour amœbæ. When isolated from the stools, they are found to have ingested red blood cells, which is an important diagnostic feature. They may be grown artificially upon special media. It is believed that amœbæ are transmitted only by contact with infected materials, such as food, water, or linens. Amœbic dysentery is best treated by careful dieting and medication with ipecac or emetin.

Other amœbæ found in the intestinal tract of man which resemble the causal agent of amœbic dysentery are: *Endamœba coli* (which is harmless), *Endolimax nana*, *Dientamœba fragilis*, and *Iodamœba williamsi*. *Endamœba gingivalis* occurs in both

healthy and diseased mouths, in decaying teeth, in the tartar at the base of teeth, and in pus pockets in the gums, which characterize pyorrhœa. In fact, this organism was considered at one time to be the actual cause of pyorrhœa. That belief has little support today, however. There are, in addition to the amœbæ here mentioned, a number of other kinds of protozoa, known as flagellates, which may be found normally in the human mouth and intestinal tract. Disease-producing flagellates, such as the trypanosomes and leishmanias, have already been discussed. No attempt has been made in this chapter to follow the disease-producing protozoa according to their descriptive classification, which is reserved for later consideration; but emphasis has fallen chiefly upon the diseases of greatest interest.

Chapter XXIV

MICROBES IN AIR AND WATER

I. MICROBES IN THE AIR

It is just as well for our sanity that, knowing the disease-producing powers of microbes, we cannot see them about us. Even their invisible presence is sufficiently disquieting — for the air is laden with microbes. Such a statement, however, requires considerable qualification. The number and kind of microbes in one locality may vary strikingly from those of another locality. The higher, the fewer — as it will be remembered Pasteur demonstrated in his classic Alpine climb. Microbes are inevitably associated with dust, consequently fewer are to be found as the air becomes purer as on the mountain-tops and over the sea. There are fewer in country places than in crowded cities; fewer in the home than in the theatre; and fewer in well-ventilated than in poorly ventilated rooms.

The following table from Marshall's *Microbiology* (third edition, page 307) gives point to these observations:

Locality	*Number of organisms per cubic metre*	*Observer*
Outdoor air, Boston	100–150 bacteria 50–75 moulds	Sedgwick & Tucker
Open air	100–150 bacteria	Fischer
Open field	250	Uffelman
Seacoast	100	Uffelman
Mountain altitude, 200 metres	0	Pasteur
Mont Blanc	4–11	Ellis
Spitzbergen (Arctic regions)	0	Levin
Middle of Paris	4,000	Ellis
Paris street	3,500	Fischer
Tailor's room in Whitechapel	17,000	Ellis
Boot Workshop	25,000	Ellis

Whence do the air-microbes come? From the soil, chiefly. Winds blow the dust from the earth's surface into the air. Rain washes microbes out of the air and deposits them back on the ground. If the surface is moist, there is little dust, and in consequence few microbes are loosed; if the surface is dry, then the particles are easily set in circulation by air in motion. Both of these factors, dryness and motion of the air, must be considered. Thus a closed room which is dry may have many microbes in it, but there is little danger of inhaling them until the air is set in motion. The air in a sewer is practically free from microbes, even though the surface teems with them — because the surface is wet. But beat a carpet, or sweep a street with a dry broom and myriads of microbes are whirled into the air which the passer-by must breathe. The noted columnist F. P. Adams campaigns against dry sweeping on a sound bacteriologic basis.

Microbes in the air are for the most part harmless to man, since they come from the soil, which harbours relatively few disease-producing organisms. Some dangerous microbes, of course, do contaminate the air, coming as they do from infected men and animals. But these are no longer the peril they were once considered. Lister, in the days when microbes first commanded respect, had his operating-room sprayed with carbolic acid. Nowadays we think less of the air-microbes and more of our pretty nurses.

Normally exhaled breath contains no microbes, since it comes over moist surfaces. There was a time when it was believed that all contagious diseases were carried by the air. But, to quote Rosenau, "with the increase of our knowledge concerning the modes of transmission of infection the list of air-borne diseases has steadily dwindled. The theory is reluctantly given up, for it is the easiest method of explaining the spread of the readily communicable diseases. There are only two diseases of man, viz., smallpox and measles, which may possibly be air-borne, in the sense that this term is generally used. Both these diseases are so readily communicable, that the virus seems to be volatile; it is assumed that the active principle is contained in the expired breath; however, there is no proof of this assumption, and some evidence to the contrary. Further, it is noteworthy that we are still ignorant of the causes and the precise mode of

entrance of the contagium in both measles and smallpox. Even in these two diseases the radius of danger is much more limited than was once supposed to be the case. The more the transmission of the communicable diseases is studied the less the air is implicated. The fact that malaria (bad air), yellow fever, and other diseases are conveyed by mosquitos has robbed the air itself of false accusations, and given a death blow to miasmas, effluvia, and intangible theories."

Microbes do not multiply in the air because there is usually insufficient food and moisture for them. Sunlight kills them. The danger from microbes in outdoor air is therefore negligible. Contagious hospitals, for example, are no menace to the neighbourhood, as Chapin has shown. And Rosenau states: "In fact, the communicable diseases are not conveyed from ward to ward or even from bed to bed in well managed hospitals." It is in crowded and poorly ventilated rooms, offices, or public conveyances that droplet infection may occur. An unprotected sneeze or cough from a person harbouring the germs of pneumonia, influenza, tuberculosis, or diphtheria throws a number of droplets containing these disease-producing bacteria into the air which others must breathe. Covering the mouth and nose when sneezing and coughing is not only good form, but a hygienic necessity.

The determination of the kind and number of microbes occurring in air may be carried out in a variety of ways. The simplest method is to uncover Petri dishes containing nutrient agar, permitting the microbes to fall upon the surface of the agar. Each microbe develops into a colony. When the colonies have developed during a suitable incubation period, they may be counted with the naked eye. Each colony then represents the progeny of a single organism. And each species of microbe may be studied and identified in the manner described in chapter III.

There are other special and more involved methods which have been devised for determining the number of microbes in air. Such methods are more exact since they deal with measured volumes of air, which are filtered through sterile sand or some other material. In general, it is well to remember that the air does not possess a microbial flora of its own, but rather depends upon the microbes present in the immediate surroundings and more particularly in the soil.

2. MICROBES IN WATER

Microbes are to be found in water, no matter how clear it seems to be; just as they occur in air. Jordan says: "The bacteria in air are not under suitable conditions for multiplication but are simply floating about in the forlorn hope, so to speak, that a chance breeze may waft them to a favourable environment; in soil the conditions for development occur only at certain times and places, and in the long run are adapted only for particular species; in water, on the other hand, a proper temperature and abundant food-supply often coexist and permit the development of a rich and varied bacterial flora. Add to this the fact that many kinds of bacteria are washed into water from air and soil and from the living and dead bodies of plants and animals, and it is seen that almost any germ, pathogenic or saprophytic, might be occasionally or exceptionally found in water. At all events, it is clear that, large as is the number of bacteria that succeed in thriving in water, a far larger number must from time to time make their way into it, to survive there for a longer or shorter period."

Some waters are badly contaminated; others are pure. Rain, often thought of as the purest water, is far from being so, for, in descending, it carries with it the dust and microbes in the air. When the air is filled with dust, more microbes are gathered than when the air is comparatively free from dust. Thus in the first few hours of a storm, rain contains more microbes than in the last hours. It has been estimated that with a yearly rainfall of twenty-four inches (which is moderate) the rain washes down some five million microbes per square yard. Snow and hail are similar to rain, except that ordinarily they carry down a larger number of microbes.

Of all natural waters the open sea and springs are perhaps the purest. Lake or upland surface waters are usually purer than rivers. The latter, like streams and ponds, depend chiefly for their microbial flora upon the amount of sewage or vegetable debris emptied into them, temperature, etc. Running water always tends to purify itself — stagnant water aids the growth of microbes. Colder temperatures tend to inhibit microbial development. But it must be remembered that there are

certain kinds of micro-organisms which can live in glaciers, and others which can survive in the hottest of natural hot springs. In general, spring-waters harbour harmless microbes, if any, providing that they are guarded from sewage pollution. The same is true of deep wells, artesian or otherwise. Shallow wells, such as abound in agricultural communities, on the other hand, are frequently contaminated by waters which drain through stable-yards, latrines, or other accumulations of refuse. The following table showing the occurrence of bacteria in different waters is after Jordan:

Source	*Number of colonies per cubic centimetre*			*Authority*
Thames River	277 (April)	–	2075 (Jan.)	Houston
Illinois River at Ottawa (about 55 miles below mouth of Chicago Drainage Canal)	6300	–	8200 (May)	Jordan
Potomac River	750 (May)	–	11,500 (Mar.)	Longley
Mississippi River at New Orleans	805 (Aug.)	–	3,597 (April)	Weston
Loch Katrine	74			Frankland
Lake of Lucerne	8	–	51	Frankland
Lake Michigan near Chicago	68	–	2000	Jordan
Deep Well-waters	0	–	12	Prescott & Winslow
Spring-water (av. of 54 samples)	41			Mass. State Board of Health
Sewage (Boston)	712,000 (Dec.)	–	11,487,500 (Sept.)	Winslow

It is sewage which supplies water with the disease-producing microbes. Typhoid fever is the best known of the water-borne infections. Unless the typhoid-fever bacilli eliminated from the intestinal and urinary tracts of the infected patient are killed by disinfectants, they may be carried by sewage and contaminate water which is used for drinking or the preparation of food. In this way epidemics ensue. Obviously, the kind of microbes present in any water-supply are far more important than mere numbers. Thus the presence of typhoid-fever bacilli or cholera vibrio is alarming, while that of *Bacillus subtilis* is negligible. It is extremely difficult to determine the former in any given water sample, chiefly because of the great dilution. In other words, there may be only a few disease-producing microbes in a large quantity of water and it is impracticable to analyse a very large sample of water in the laboratory. Consequently an indirect method is used — namely, the determination of the presence of *Bacillus coli* (see page 127), which is generally regarded as a satisfactory index of pollution.

Where *Bacillus coli* is present *Bacillus typhosus* is not far behind. To be sure *Bacillus coli* does not always occur in water solely as a result of human contamination, for it is a common and harmless inhabitant of the intestinal tract of many domestic animals; but the presence of *Bacillus coli* in appreciable numbers is suspicious. According to Rosenau, if more than ten colon bacilli per centimetre are found, the water must be considered dangerous for human consumption and should be unqualifiedly condemned.

Sanitary control and purification of the water-supply, as well as the adequate disposal of sewage, are imperative to safeguard

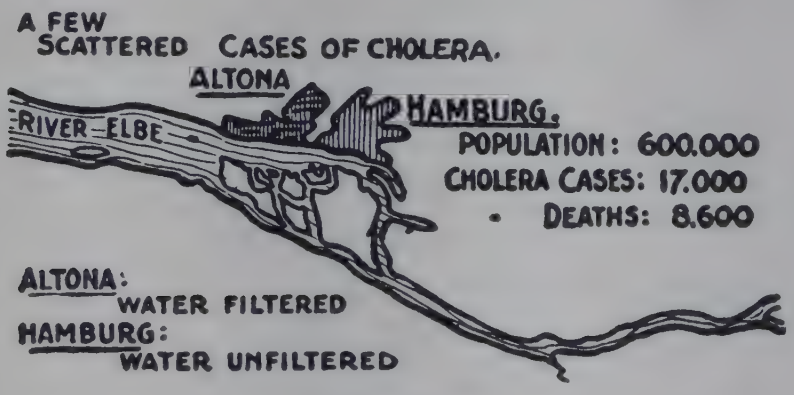


FIGURE 106

An instructive contrast between Altona and Hamburg (Germany) before the latter filtered its water, having learned its lesson from a sharp outbreak of cholera. (After Marshall.)

the health of the community, for there are few sources in modern civilized areas which are not subject to pollution. The installation of equipment for purifying water is now an item in the budget of every large city. There are several methods of purifying water and sewage — namely, by sedimentation and filtration, by ozone, and by various chemicals. Purification by sedimentation and filtration has been in use for over a hundred years. Koch pointed out that Hamburg, as a result of drinking unfiltered water from the river Elbe, suffered a severe cholera epidemic, while the town of Altona was spared because it filtered the water coming from the same source. (See fig. 106.) The procedure of purification by sedimentation and filtration is first to store the water in large reservoirs. This permits the heavier particles and vegetable matter to settle out. After storage the water is filtered through sand, gravel, and pebbles,

which remove from 97 to 99.5 per cent of all the microbes. (See fig. 107.) The following table, after Marshall, is impressive:

MEAN OF MONTHLY EXAMINATION FOR THE YEAR

	Micro-organisms per cubic centimetre		
	At source	*After storage*	*After filtration*
London, Lambeth Works...	16,138	7,820	75
London, Chelsea Works....	16,138	1,067	34
Berlin, Lake Müggel.....	1,400	....	60
Paris, Marne.....	79,000	....	630
Paris, Seine.....	186,986	....	400

This principle of sedimentation and filtration should govern the construction of all farm wells. Wells should never be located nearer than a hundred feet to where the surface drainage from cesspools or stables can reach them. Contrary to popular belief, wells are only infrequently polluted by subsoil drainage. Surface drainage should be away from the well, and the latter should be situated on a good slope. To quote Marshall: "All water entering such a well must percolate through a considerable depth of soil, and undergo purification."

Another method employed for precipitating out microbes, soil, and vegetable matter is to add a coagulant, such as basic sulphate of ammonia, to water stored in reservoirs for six to twenty-four hours. In the home, water may be purified by filtering or by boiling. Boiling, however, gives to the water a flat, insipid taste, due to the fact that the dissolved gases, particularly oxygen, have been driven off. Cooling and shaking boiled water does much to restore its natural palatability.

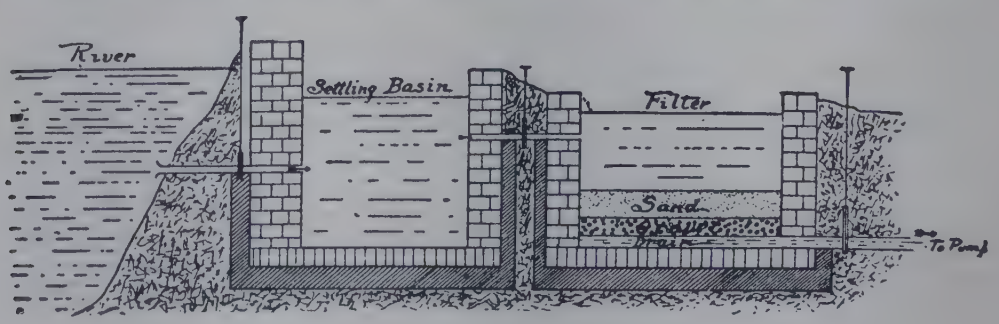


FIGURE 107

A filtration plant in cross-section. (After Jordan.)

The addition to water of small amounts of chemicals such as chlorine compounds, or of gases (chlorine, ozone, etc.) is widely practised. In fact, the chlorination of water is increasing so much in popularity that it is becoming the method of choice for the large cities in the United States.

The disposal of sewage is of such importance in its influence on the water-supply that it is worthy of more than passing recognition. Sewage is of necessity highly complex in character. It represents the accumulation of human excreta, refuse, factory wastes, etc., and its composition varies with the chief sources of supply. So does its microbial flora. In the past, sewage was dumped into some body of water and promptly forgotten; but when such contaminated water was drunk without previous filtration, epidemics were frequent.

Just as water is purified by sedimentation, filtration, and the addition of chemicals, so sewage can likewise be purified. Sewage is often passed through screens in an effort to effect mechanical separation of fluid from sludge. Sedimentation in tanks ("septic," Imhoff, etc.) has also been employed. Precipitation of the heavier elements of the sewage with alum or other chemicals yields a clear liquid, but the sludge which remains is practically worthless. Contact and trickling beds, where the sewage runs through sand or coarser material, are effective because they oxygenate the sewage. But none of these methods is altogether satisfactory.

The newest method in treating sewage aims at the production of "activated sludge," which can be used as a fertilizer on farm land. This is accomplished by aerating successive batches of sewage with a continuous bubbling stream of air. The advantages claimed for this method, according to Conn and Conn, are: "(1) Organic material is converted almost wholly into nitrates and other inoffensive soluble materials and odourless gases; (2) the quantity of sludge produced is small; (3) the sludge is a good fertilizer."

Microbes in nature are to be respected. They need be feared only when they are not controlled.

Chapter XXV

SOIL MICROBES

Soil microbes are the friends of man; for man, like all other animals, requires some vegetable matter for his sustenance. And plants grow in soil. The process of decay, brought about through the agency of microbes, makes food available for plants, thereby furnishing one of the most important factors in the life cycle of plants, animals, and man.

"Sedgwick, the pioneer of American public-health activities, spoke of the 'living earth' in the sense that it is teeming with life; bacteria, moulds, amœbæ, and many of the primitive forms of the animal kingdom, as well as worms, insects, snakes, birds, rodents, and many other animals, make their temporary or permanent homes in the upper layers of the earth" (Rosenau). The soil is indeed an excellent culture medium for microbes. As in the laboratory, a number of factors determine microbial existence in the soil — namely, food-supply, moisture, temperature, oxygen, acidity, etc. That such factors vary in different soils should be apparent. Thus, one soil may have more of one kind of mineral than another, depending on the underlying rock. Granite yields more potash, for example, than sandstone; limestone yields more lime than shale, etc. Soils rich in vegetable matter, such as those found along river beds, furnish more food for microbes than the sandy soils that border the ocean.

Soil moisture is largely determined by the composition of the soil and the rainfall. Fine-grained soils, such as heavy clay soils, retain their moisture much better than do coarse-grained sandy soils. The greater the rainfall, the more moisture in the soil; and moist soils are richer in microbes than dry soils. Warmer temperatures also favour most important forms of microbial development; colder temperatures retard them. An abundance of oxygen, as in sandy soils, stimulates the growth of aerobes; in a poorly ventilated soil the anaerobes are favoured. If the soil becomes too acid as a result of impoverishment or failure to

supply lime, microbial development is not so rapid as when the reaction is nearer alkalinity.

Microbes flourish only in the upper layers of soil. As we descend, the microbial population decreases, owing to the absence of the favourable conditions just described. In general, the soil microbes are not capable of producing disease, although the soil does, of course, harbour tetanus bacilli and other harmful bacteria. But the latter constitute only a small fraction of the total number. As Rosenau says: "It requires a bacteriologist to tell the difference between clean dirt and dirty dirt. We lack a sixth sense, or microscopic eye, to see and distinguish the harmful germs."

At one time it was thought that the burial of persons who had died of infectious diseases was a menace. It appears, however, that this fear was greatly exaggerated, for it has been demonstrated that cholera or typhoid bacilli cannot be recovered three weeks after burial, nor can tubercle bacilli be found after three months. This is not to say, however, that drainage from a cemetery will not pollute near-by wells, for such an occurrence has been frequently observed.

It is difficult to determine the kind and number of microbes growing in any particular soil. The usual microscopic and plating methods yield only an approximation, since it is almost impossible to duplicate the conditions under which the microbes live there normally. Very short non-motile rods are usually to be found in abundance, as are Actinomyces (higher bacteria). Spore-forming rods, notably *Bacillus cereus* and *Bacillus mycoides*, are encountered, as well as such other forms of microbial life as moulds, algæ, and protozoa. Garden soil has been found to harbour from 14,000,000 to 225,000,000 bacteria per pound of soil, while an arid soil in the South-west, for example, averages one-tenth of these numbers.

The activities of microbes in the soil are manifold. First, they play an important rôle in Nature's carbon economy. Carbon comes to plants from the carbon dioxide of the atmosphere. Animals get their carbon from plants. Microbes break down animal tissues to carbon dioxide, which is returned to the atmosphere, whence the plants again obtain it, making the cycle complete. Furthermore, microbes break down plant

tissues, which are themselves not always available as food for animals; but other plants, which can be utilized by animals, thrive. Thus the microbes are of value to animals indirectly. The carbon compounds decomposed by microbes in the soil include sugars, starches, waxes, gums, and cellulose. The following illustration (see fig. 108), taken from Marshall, is a diagrammatic representation of the carbon cycle; the heavy arc emphasizes where microbial activity is most important.

The nitrogen cycle (see fig. 109) is similar to the carbon cycle, but more complicated. In describing the former it is impossible

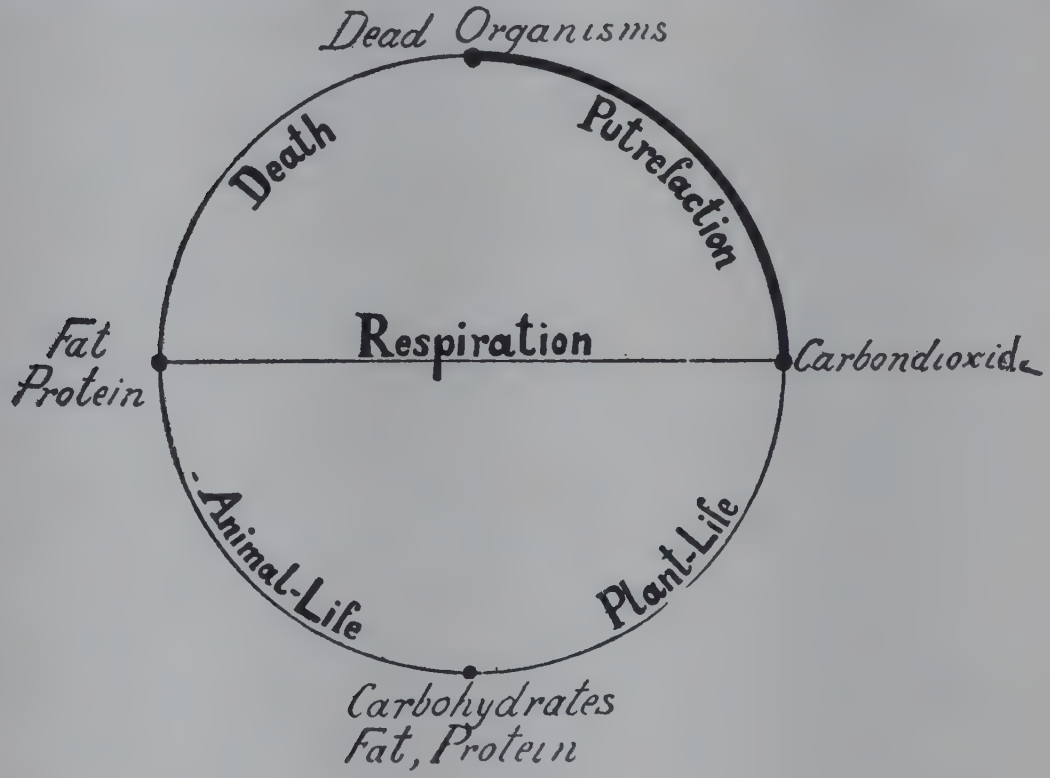


FIGURE 108

The carbon cycle. (*After Marshall.*)

to avoid the use of certain chemical terms. Plants take nitrogen from the soil in the form of salts called "nitrates." This mineral form of nitrogen is changed in the plant tissues into protein, which is a complex combination of nitrogen, carbon, and other elements. Plants are eaten by animals, digested, and excreted as urea and hippuric or uric acid. The microbes decompose the latter into ammonia (the gas). Only a part of the protein is excreted by the animal, however, the remainder being stored in the tissues. Upon the death of the animal the carcass is decomposed by microbes, ultimately into ammonia. Other bacteria utilize ammonia as a food and transform it into nitrates and

nitrites by a process known as "nitrification." Then the plants complete the cycle by utilizing the nitrates thus formed.

But there are two features complicating the nitrogen cycle still to be mentioned. Firstly, there are certain bacteria which can decompose nitrates, liberating nitrogen gas in a process known as "denitrification." Secondly, to compensate for this loss, there is another still more important group of bacteria which have the remarkable capacity of fixing free nitrogen

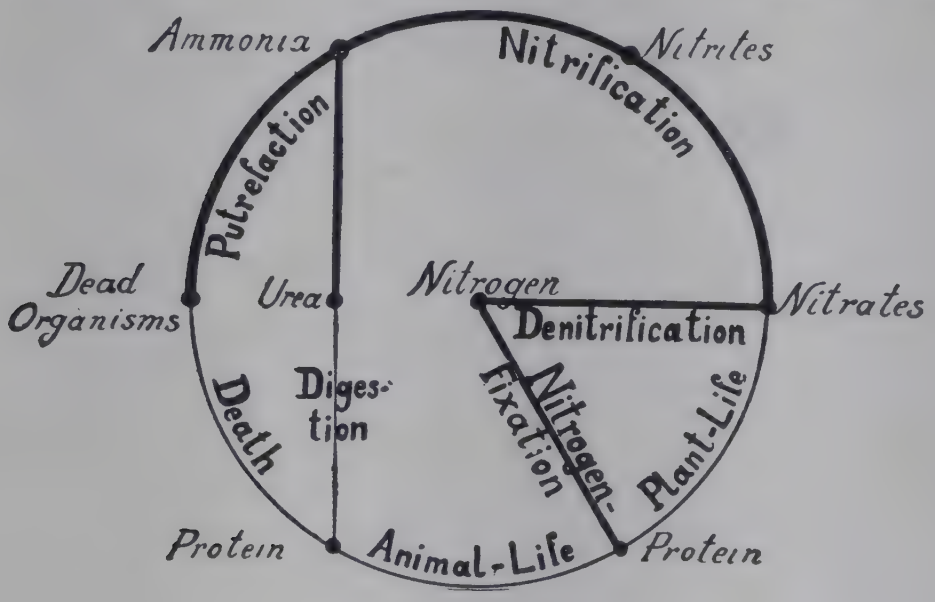


FIGURE 109

The nitrogen cycle. (After Marshall.)

from the atmosphere. The nitrogen cycle is thus complete. The sulphur cycle is analogous. (See fig. 110.)

Nitrogen-fixation is of such great economic importance that it deserves special mention. It had long been observed in agricultural practice that the growth of legumes (that is, peas, beans, clover, and alfalfa) enriches the soil, as well as yields a valuable crop. The explanation for this phenomenon was not apparent until Hellriegel and Wilfarth in 1886 demonstrated that the nodules which grow upon the roots of legumes contain a special kind of bacteria which have the power to absorb nitrogen directly from the atmosphere and fix it in the roots of the growing plant, thus supplying to the plant the most expensive fertilizer constituent, nitrogen, at no expense whatsoever. The plant supplies food for the bacteria; the bacteria fix nitrogen for the plant. It would be difficult to find a more perfect example of symbiosis — that is, living together to mutual advantage.

FIGURE 110

The sulphur cycle. (After Marshall.)

The nodules on the roots of a legume may be cut open and the bacteria contained therein isolated on special media. (See fig. 111.) In a practical way a knowledge of bacteriology is of assistance in growing a good crop of legumes, for the soil may be artificially inoculated with cultures of nitrogen-fixing bacteria best adapted to the legume in question. Such a procedure yields a bigger and better crop than one grown without such aids. It

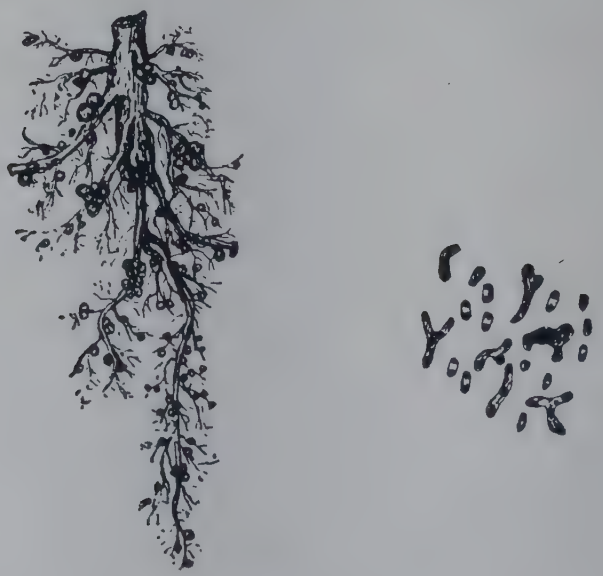


FIGURE 111

Legume nodules on plant roots, at the left. Nodule bacteria, at the right. (After Conn and Conn.)

should also be mentioned that there are still other bacteria which can fix nitrogen in the soil independently of plants or non-symbiotically. (See fig. 112.)

The proper handling of the soil by cultivation, fertilization,

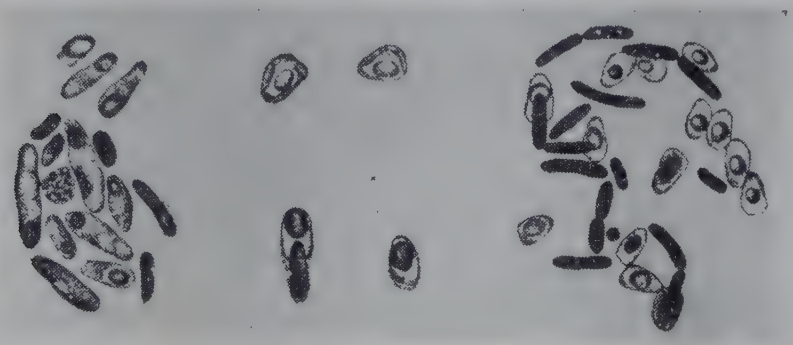


FIGURE 112

Non-symbiotic nitrogen-fixing bacteria. (After Marshall.)

liming, crop selection, and sterilization accomplishes much in influencing the microbial population as well as in improving plant growth. Soil microbes, as has been shown, play an important rôle in agriculture. Their development should be stimulated as much as possible. Yes, soil microbes are the friends of man.

Chapter XXVI

MICROBES IN MILK

I. RAW AND PASTEURIZED MILK

Milk is known as "the perfect food." The microbes find it so, fully as much as man. And for this reason milk is responsible for more illness and death than perhaps all other foods combined. Microbes grow readily in milk; consequently a very slight contamination may be widely disseminated. Milk is of all foods probably the most difficult to collect, handle, ship, and distribute in a clean, fresh, and satisfactory state. Milk is the most easily spoiled of all our foods. Milk is the only universal article obtained from animal sources which is consumed raw. All of this means that even under the most favourable circumstances in the drinking of milk many microbes are ingested.

These are harsh words when one stops to consider that milk as it is secreted in the milk gland of the cow, "which has become the wet-nurse of the human race" (T. Smith), is in all probability entirely free from any bacteria. But when it reaches the udder, milk becomes contaminated, since bacteria get into the udders from without. If milk were perfectly handled after leaving the udder, the microbial content would be negligible, but it rarely is. Opportunities for gross contamination abound. Unclean milking-utensils, imperfectly sterilized pails, cans, and milking-machine equipment, together with filth from the cow and lack of cleanliness on the part of the milker, are responsible for the presence of a large number of microbes in freshly drawn milk.

The handling of milk after it has been collected has much to do with its keeping quality. The three factors which enter into the keeping quality of milk are: its initial microbial content, the temperature of storage, and the duration of storage before consumption. Increase the intensity of any of these factors, and milk spoils rapidly; reduce the initial microbial content by cleanliness, keep the milk iced, and hold it for only a short period of time, and the milk is unquestionably a safer food.

There are certain types of bacteria which predominate in milk — namely: spherical organisms closely resembling the pus-forming staphylococci and streptococci, the chief representative of which is *Streptococcus lacticus* (synonymously termed "*Bacterium acidi lactici*"); the colon-ærogenes group of bacilli; and lactobacilli, chiefly represented by *Lactobacillus bulgaricus*. (See figs. 113, 115–17.) All of the above bacteria sour and curdle milk. That is, they attack milk sugar (lactose) to form lactic acid, which in turn coagulates the milk. (See fig. 114.) The more bacteria present initially, the quicker does the milk sour and curdle. Low temperatures tend to preserve milk; higher temperatures accelerate spoilage.

FIGURE 113

Types of bacteria found in milk. A, lactic-acid bacteria; B, streptococci; C, cocci; D, B. coli; E, L. bulgaricus. (After Conn and Conn.)

To prevent milk from spoiling, it is usually pasteurized — that is, heated for a short period of time and then cooled. The heating process kills most of the living bacteria; the cold retards

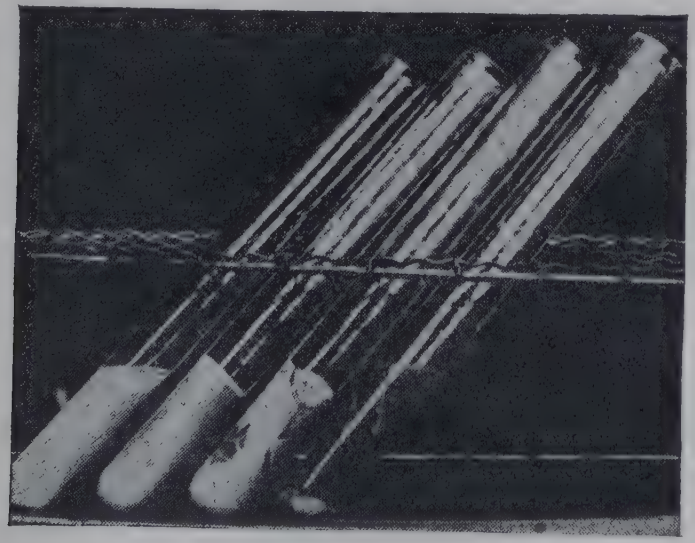


FIGURE 114

Effect of different kinds of bacteria on milk. From coagulation to peptonization. (After Conn and Conn.)

the further multiplication of the survivors. Chemicals are sometimes used, but such practice is contrary to the pure-food laws of the United States. Pasteurization is really an excuse for insufficient cleanliness. Thus, if cows are healthy, if utensils are

FIGURE 115

Colonies developing upon an agar plate held for ten seconds below udder which was gently brushed with the hand. (After Marshall.)

FIGURE 116

Colonies developing upon an agar plate from a bit of dust found in a cow stable. (After Marshall.)

sterilized, if filth from cow or milker is not permitted to enter the milk, and if the milk is promptly cooled after milking, then the bacterial content is insufficient to cause any concern.

When milk is collected under the most favourable conditions, it is unnecessary to pasteurize it and it is sold as certified milk. As a rule, the highest grade of milk (grade A) contains less than ten thousand bacteria per cubic centimetre (roughly one-thousandth of a quart) after pasteurization and is intended for babies, invalids, and those who are satisfied with nothing less than the best. Grade B milk, that most popularly consumed, is pasteur-

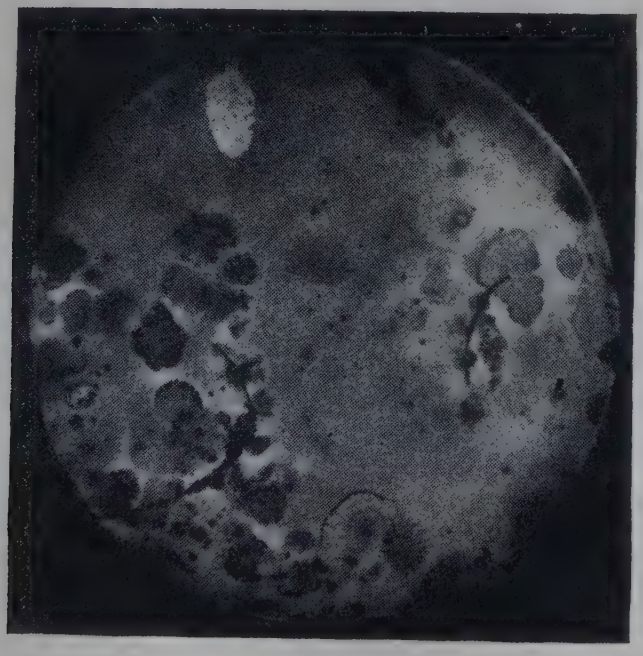


FIGURE 117

Colonies developing from cow hairs planted on the agar plate. (After Marshall.)

ized milk which should contain less than fifty thousand bacteria per cubic centimetre. Grade C milk is also pasteurized, but is on the point of souring and should not be taken raw. It may, however, be used for cooking purposes. It should not contain more than a hundred thousand bacteria per cubic centimetre. These standards vary in different cities.

There can no longer be any question as to the value of pasteurization in reducing the bacteria in milk and the consequent conservation of health as compared with drinking raw milk. Park and Williams have published the following significant table of observations on the comparison of the same raw and pasteurized milk when fed to babies for two summers:

Kinds of milk (number of bacteria when consumed)	*No. of infants*	*Remained well for entire summer*	*No. having severe or moderate diarrhœa*	*Average No. days off milk during summer*	*Average weekly gain in weight oz.*	*Average number of days diarrhœa*	*Deaths*
Pasteurized milk, 1000–50,000 bacteria per c.c.	41	31	10	3.0	4.0	3.9	1
Raw milk, 1,200,000–20,000,000 bacteria per c.c.	51 [1]	17	33	5.5	3.5	11.5	2

[1] Thirteen of the fifty-one infants on raw milk were transferred before the end of the trial to pasteurized milk because of serious illness. If these infants had been left on raw milk, it is believed by the writers that the comparative results would have been even more unfavourable to raw milk.

The bacteriologic control of milk is of utmost importance. The microscopic and plate count determinations, as generally carried out, yield a satisfactory index of the purity of milk. When milk is impure, epidemics of infectious diseases frequently occur which can be traced directly to that source. Among the milk-borne diseases may be mentioned tuberculosis, typhoid fever, scarlet fever, septic sore throat, and bacillary diarrhœa. With the increasing concentration of the population in large cities the problem of an adequate milk-supply becomes more difficult. Wider and wider territories must be tapped and controlled to yield sufficient fresh milk for city consumption. The public owes it to itself and its sanitarians to punish immediately anyone tampering with or transgressing the laws which protect its milk-supply.

2. BUTTER

Cream, which is the fatty part of milk is less likely to become spoiled by microbes than is whole milk, but the same general bacteriologic considerations applicable to milk pertain to cream. If bacterial activity goes forward in cream, it, too, becomes sour. Butter is made by churning cream. Formerly, the custom was to permit the cream to "ripen" spontaneously, or to become sour by the introduction of pure cultures known as "starters." This imparted a characteristic flavour to the butter. Nowadays, the cream is pasteurized, and the "starter" is added to impart flavour, but bacterial multiplication is not stimulated, since the trend seems to lie in the direction of butter of milder flavour, or

sweet cream butter. Butter substitutes, made from oil instead of cream, such as oleomargarine, also depend for their flavour upon the addition of ripened cream. Pasteurization of the cream and the use of a pure-culture "starter" make for uniformity in the flavour, which would otherwise vary, as a result of the presence of a number of different kinds of microbes. Undesirable microbes in butter produce the unpalatable flavours of fish-oil, turnips, etc. The salting of butter prevents mould growth, the latter being the bane of the butter-manufacturer's existence. Just as with milk, butter is best preserved by cold.

3. CHEESE

Flavour in cheese is perhaps even more important than in butter. Cheese, as everyone knows, is made from curdled milk. When the milk is curdled by lactic acid due to the spontaneous souring of milk or by a pure culture of lactic acid bacteria, "acid-curd cheese" is formed. The whey is drained off and the cheese, which may really be considered a form of sour milk, is ready for consumption. Acid-curd cheese is usually home-made or intended for local distribution.

Most cheeses, however, are not of the acid-curd variety, but are made from milk which is curdled by the use of rennet (an enzyme preparation). Rennet-curd cheeses are classified as hard and soft. In the former category belong the familiar American, Swiss, Cheddar, and Edam cheeses. They are made by squeezing as much liquid as possible from the curdled milk and then permitting it to undergo a slow ripening process. Sometimes pure cultures are used as "starters," just as in the manufacture of butter, in an attempt to control flavour. The physical, chemical, and bacteriologic changes which occur in the ripening of cheese are extremely complex and little understood. This is exemplified by the many vain efforts which have been made to produce in the United States a Swiss cheese identical with that made in Switzerland. Not only have Swiss cattle been imported and Swiss shepherds brought over to care for them, but manufacturers have gone to the extreme of bringing Swiss water and greens to nurture the animals. All this to little avail — possibly they should have brought along an Alp or two as well.

Soft cheeses, which include Camembert, Roquefort, Gorgonzola, and Limburger, differ from hard cheeses in that the fluid portion of the curdled milk is allowed to drain off instead of being expressed. (See fig. 118.) Microbes of different kinds — bacteria, moulds, and even yeasts — are used in the production of hard cheeses. Thus the mould *Penicillium camemberti* is used in making Camembert cheese, and *Penicillium roqueforti* in Roquefort cheese. It is highly important that the ripening process be so controlled that only the desired microbe gains ascendency. Otherwise, the flavour is impaired by contaminators. This means that the curdled milk must have the desired microbe introduced into it either naturally or artificially, that care must be taken to prevent the access of foreign microbes, and that during ripening the temperature and moisture be regulated in a manner suitable to the growth of the desired mould. In localities where a particular variety of cheese is produced, as in the Roquefort region in France, the desired bacteria are indigenous, but when the same type of cheese is manufactured in another country, it is necessary to import the desired mould for inoculation of the curd.

FIGURE 118

Three types of cheese. Swiss at the left; Cheddar, center; Roquefort, at the right. (After Conn and Conn.)

4. OTHER DAIRY PRODUCTS

In addition to milk, butter, and cheese, there are many other dairy products offered to the public. Bacteriologic control of them is highly important, for an excessive number of microbes may cause spoiling and certain species induce disease. Evaporated or unsweetened condensed, sweetened condensed, concentrated, and powdered milks are consumed in large amounts. The fact that they contain little moisture reduces the possibility of bacterial development.

Sour milk, buttermilk, and especially cultured milks have

become popular beverages. The last were discussed in chapter XI. In sour milks, one expects to encounter large numbers of bacteria, but of a harmless or even beneficial variety. Danger, however, may come from contaminators, which are not properly controlled.

Ice-cream, too, varies in quality with its bacterial content, which depends chiefly upon the cream and condensed milk which enters into its manufacture. Again, the kinds of bacteria present are of greater significance than mere numbers. When ice-cream is made from cream which has been properly handled, a high count of bacteria is of little concern, because the organisms are usually members of the common *Streptococcus lacticus* group found in milk. But if the ice-cream is made from cream kept in cold storage for some time, which inhibits the *Streptococcus lacticus* group and stimulates putrefactive bacteria, then the ice-cream may cause ptomaine poisoning as a result of the toxic products formed by the putrefactive microbes.

The ease with which milk and its products are contaminated by microbes to such an extent as to render them unfit for human consumption makes it urgent that they be as fresh as possible. Danger may thus be minimized, but is not necessarily eliminated. It is not always large numbers of microbes that constitute a hazard to health; it is often the mere presence of noxious species. It is only when milk is free from harmful microbes that it can become "the perfect food."

Chapter XXVII

MICROBES IN OTHER FOODS

Microbes in food tend to make it unfit for human consumption unless certain precautions are taken. The souring of milk and cream, the decaying of fish and meat, the rotting of fruit, are familiar phenomena. Long before bacteriology became a science, experience taught our ancestors simple and effective methods of guarding food against spoiling.

Conditions which favour the growth of microbes in food, such as an optimum of moisture, temperature, or oxygen, must be considered on the one hand; and, on the other, the palatability and nature of the food to be preserved is equally important. The common methods employed for reducing microbial activity in food are by drying, heating, cooling, or adding chemical preservatives. The choice of any single method depends upon the food under consideration.

Drying food reduces its content of water so that the microbes present cannot grow. Some foods dry naturally; others must be dried artificially. In the former category belong meat, fish, and, more recently, milk and eggs. Milk and eggs are dried by spraying them into a warm vacuum, where the fine droplets dry immediately. A powder is thus formed which has good keeping qualities. It then becomes a simple matter to add the water lost by drying and establish the original fluidity. Foods with comparatively little moisture, such as syrups, molasses, jellies, jams, or oils, do not suffer from microbial activity unless an unusual supply of moisture is present.

Drying deprives microbes of their water-supply; heating kills them. Appert, a French confectioner, utilized the latter principle in 1810, and it is still in vogue. Home canning is never so safe as commercial canning or "processing" — that is, heating to temperatures above the boiling-point; for unless the spores are killed, together with all living microbes, there is danger of botulism (see page 138).

Some foods lend themselves more readily to preservation by heating than do others. Heat tends to induce physical and chemical changes which make for alteration of taste, appearance, and digestibility. Thus, milk products should not be heated to temperatures as high as those applied to fruits and vegetables. Milk products are pasteurized; while fruits, vegetables, or salmon are sterilized at temperatures above the boiling-point of water. The factors which control successful canning are: cleanliness throughout the entire procedure; soundness and freshness of raw material; pure water-supply; and proper receptacles, suitably sealed.

If the process has not been carefully controlled, canned food is likely to become spoiled. The canners speak of "swells" and "flat sours." The term "swells" refers to cans which bulge at the ends owing to the formation of gas by microbes which have not been killed. "Flat sours" are canned goods in which fermentation has taken place, causing the formation of acid. On no account should canned food which is undergoing decomposition be eaten. Taste and odour are ordinarily excellent criteria. It is dangerous to taste food from "swells," because *Bacillus botulinus* may be present where gas is produced; or where the contents of the can are mushy or disintegrated; or where an odour like that of rancid cheese is discernible. The toxin of *Bacillus botulinus* is so potent that even a mouthful of food containing it may prove injurious, if not fatal.

In addition to drying and heating, food may be preserved by cold. Low temperatures tend to inhibit and kill microbes. The cold-storage industry is consequently extensive. It is concerned with meat, fish, poultry, eggs, milk, butter, and even fruits and vegetables. There is considerable prejudice in some quarters against cold storage, as there is against canned foods. To a considerable degree this prejudice is unwarranted, since cold storage and canning make available foods which are fresh for only a short period of time. If cold-storage foods are properly labelled and branded, the consumer knows precisely what he is purchasing; for he knows how long and under what conditions the food has been stored, so that deception, as now frequently practised, may be eliminated.

Food may be preserved by the addition of certain chemicals,

as is often done with tomato products, like ketchup or Chili sauce. The pure-food laws permit the use of salt, sugar, spices, or vinegar, provided these ingredients are specifically mentioned in the label. There are many tricks of the trade employed to enhance the appearance or taste of various articles. So long as the consumer is informed of the chemicals used for such purposes, the responsibility falls upon his own shoulders. Thus, few of us object to the use of salted fish, cured ham, or pickled products. But not all of us inspect labels carefully enough to realize that "butter coloring is quite generally used to produce the color of June butter the year around; nitrates bring about a pleasing red color in cooked pickled meats; copper sulphate is used to give a more brilliant green color to prepared vegetable foods; sulphites restore the red color of freshly cut meat to meat far from fresh; saccharine devoid of food value gives a taste resembling sugar to a variety of preparations at a great saving in cost to the manufacturer; carbonates of the alkalies or alkaline earths, added to milk, neutralize the acids resulting from bacterial decomposition and so keep milk sweet; inorganic acids added to weak vinegar increase its acidity. Some of these practices are so universal and so well known that they are no longer criticized; others, such as the use of chalk in milk, are generally disapproved" (Marshall).

The fight for pure foods knows many champions and more quacks. The public is too easily impressed by a smattering of chemistry, punctuated by some tongue-twisting technical terminology. The self-advertising "pure food" specialist is seldom without an interested motive. Those who are really concerned with the public health, such as Dr. Harvey W. Wiley, have been thorns in the side of manufacturers of adulterated food products and have never profited directly or indirectly by the sale of this or that commodity. The United States Government maintains laboratories for the analysis of foodstuffs. As a result of such analyses much food has been condemned and ordered destroyed, or means have been taken to enforce the law which forbids the sale of food declared by the federal laboratories to be unfit for human consumption. The Food and Drug Act, like all other legal measures, has certain imperfections which enable the unscrupulous manufacturer to market borderline products.

Where medical authorities disagree, as, for example, with regard to the harmful effects of saccharine, shysters rush in to make profits. So long as business interests control food production, the public will never have the benefit of scientific doubt.

Chapter XXVIII

ALCOHOLIC BEVERAGES

It would be a difficult, and in this day an altogether too depressing task, to list all the alcoholic beverages. One and all, they are the products of microbial activity, chiefly yeasts. Grape-juice, technically known as "must," when fermented,

Figure 119

Bacteria of slimy wine. A, B, C, pure cultures of various forms; D, mucilaginous sheath of slime bacteria. (After Marshall.)

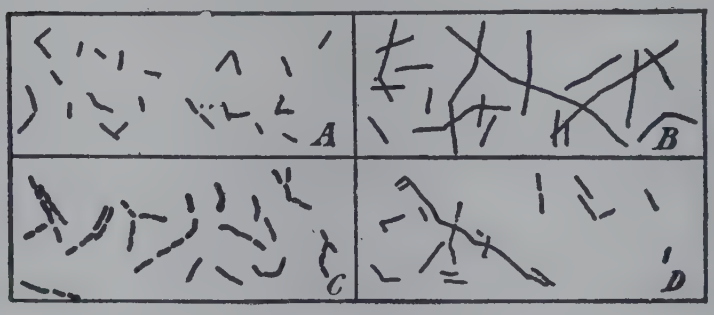


Figure 120

Bacteria of wine disease. A, bacteria of "turned wine," young wine; B, bacteria of "turned wine," old wine; C, mannitic bacteria; D, bacteria of bitter wine. (After Marshall.)

becomes wine. Grape-juice contains from twelve to twenty-five per cent of fermentable sugar and furnishes an excellent medium for the development of yeasts and moulds, but is not especially well adapted to the growth of bacteria. When the ripe grapes are brought in from the vineyard, moulds and yeasts, together with bacteria, are to be found upon the skins. The moulds and bacteria, however, are undesirable, for they are likely to pro-

duce fermentations which impair flavour and result in insipid, slimy, *mousy*, *turned*, and cloudy wines. (See figs. 119, 120.)

The art of wine-making lies in controlling microbial development in such a way that only the true wine yeast desired gains ascendency. Good practice calls for cleanliness and care in handling the grapes to avoid bruising; rapid crushing; settling and decantation of the grape-juice at low temperature; and treatment with sulphur fumes to eliminate dust and impurities of all kinds. Then, as in butter-making, a "starter" of a tested yeast culture or especially selected grapes is added to ensure the development of the desired yeast. *Saccharomyces ellipsoideus* is usually the yeast which predominates at the end of the fermentation process. The temperature at which fermentation progresses establishes to a considerable degree the quality and character of the wine. Thus, for light and white wines the maximum temperature should not exceed 77°F., for heavier wines 86°F., for heavy red wines 95°F.

The colour of white and red wines depends upon the colour of the grapes used and whether or not the skins are removed before crushing. The difference between dry and sweet wines is that in the former the sugar present in the original grape-juice is entirely consumed or fermented by the yeasts; while in sweet wines fermentation is stopped before all the sugar is consumed, or extra sugar is even added. After fermentation the wine is drawn off into clean casks and stored at a cool temperature. It is further clarified, or *fined*, and then allowed to age. The kind of grapes used, the yeast, and the ageing process determine the bouquet of any wine, which brings to the connoisseur a rare and indefinable delight.

Sparkling wines or champagnes, which release their captive bubbles when the cork pops, contain considerable carbon dioxide gas in solution, present in ordinary soda-water. *Fortified* wines are those to which alcohol has been added over and above the amount produced during fermentation. Vintage wines are the prized wines of particular years when the bouquet is perfect for the wine under consideration.

Wine is not the only alcoholic beverage prepared from fruit juice. The same principles of fermentation may be applied to apple-juice, which yields cider; or pear-juice, which yields

perry. Yeasts similar to or identical with wine-making yeasts may be employed.

Beer, as anyone who has lived near a brewery can testify, is made from cereal grains, chiefly barley, corn, and rice. Since these contain no sugar, it is necessary first to transform the starch, of which there is an abundance, into sugar. This is accomplished by *malting* — that is, soaking the grain in water; keeping it at a low temperature for several weeks, while the grain sprouts or germinates; and then drying. Incidentally, malt syrup made from either brewers' or bakers' malt has a high food-value and enters into many tonics. The malt is crushed, water and usually sugar are added, and heat is applied. This is known as "mashing." In this stage the enzymes formed during malting convert the starch to sugar, and the solution is termed "wort." Yeast is added, usually of the *Saccharomyces cerevisiæ* group or *Torulæ*, and the wort is fermented into beer.

The best-known varieties of beer are *lager*, fermented with bottom yeasts; *ale*, fermented with top yeasts (and *Torulæ*); and *porter*, similar to ale, but darker in colour, as a result of using caramelized malt. Near beer, or non-alcoholic beer, is nothing more than wort which has not been allowed to ferment, or beer from which the alcohol has been removed. As in wine-making, the control of fermentation in the manufacture of beer is of prime importance and depends upon cleanliness and regulation of temperature. Further steps in the process are clarification, bottling, and pasteurization. Imperfections in raw materials and laxity in bacteriologic procedure result in abnormal flavours or cloudiness, with consequent economic loss.

Ginger-beer is made by the fermentation of sugar solutions to which pieces of ginger root and ginger-beer plant are added. The Japanese make *saké*, or rice beer, by the fermentation of rice with moulds and yeasts. Pombe is an African beer made from millet seed. Mead, a favourite alcoholic beverage of eastern Europe, is made by the fermentation of honey dissolved in water.

Distilled alcohols are prepared from sugar or starch contained in various plants and fruits. When sugary substances are used, the principles of wine-making are applied; when starchy substances are used, brewing practice is followed. Brandy is

made from grapes; rum from sugar-cane; and whisky from rye or other grains. Most industrial alcohol is made from beet molasses. As in wine-making and brewing, yeasts are employed to ferment the sugars. After the alcohol is produced in the fermentation process, it is driven from the solution by the application of heat (alcohol has a lower boiling-point than water), and the alcoholic vapour condensed by chilling. This process is known as "distillation." Distilled alcoholic beverages are aged in wooden casks to give them a choice flavour.

Distilled alcohol may be used as a basis in the preparation of many alcoholic beverages, such as gin, cordials, etc. In these days of prolific prescription-writing, it might be well to remember that alcohol is really of great value to medicine. It has, further, extensive application as a solvent in industrial chemical processes and may also be used as a source of fuel.

Chapter XXIX

MICROBES HARNESSED TO INDUSTRY

I. VINEGAR

If wine or any other liquid containing alcohol be exposed to the air so that film gathers on the surface of the liquid, the alcohol is replaced by acetic acid and vinegar is formed. The acetic-acid-forming bacteria usually accomplish this feat.[1] (See fig. 121.) From the standpoint of the wine-manufacturer these organisms are most undesirable, but the vinegar-manufacturer, on the other hand, prizes them highly. Originally vinegar was made only from wine — in fact, vinegar means "acetified wine." But now any alcoholic liquid may be used, whether it comes from the fermentation of molasses, honey, malt, fruit juices, cider, or vegetables such as corn, potatoes, or beets.

FIGURE 121

Types of vinegar (acetic-acid) bacteria. (After Conn and Conn.)

The first step in vinegar-making is the production of alcohol by means of yeast fermentation. The quality of the raw material used determines the quality of the vinegar which will be produced. The second step consists in adding to the alcoholic liquid some nutritive substance (such as malt extract), water, and some good vinegar, which usually contains enough acetic-acid bacteria to act as a "starter." Aeration and proper temperature are highly important during the acetic-acid fermentation. There are several ways of carrying forward the fermentation under the best conditions. These are variously known as the "domestic," "Orleans," "Pasteur," "rapid," and "rotating barrel" methods. (See fig. 122.) When the fermentation has been completed, the vinegar is filtered and usually coloured slightly

[1] They are called "*Mycoderma aceti* of Pasteur," "*Mycoderma vini*," "*Bacterium aceti*," "*Bacterium pasteurianum*," "*Bacterium kützingianum*," and "*Bacterium xylinum*."

with caramel. Wine and cider vinegars, which have the best flavour, are usually filtered, pasteurized, and aged. By far the greatest quantity of liquid sold as vinegar is nothing more than diluted acetic acid made commercially from distilled alcohol, to which flavouring and colouring-matter are added. It has therefore only a slight resemblance to true vinegar, which should have a real bouquet.

As in all fermentation processes, the entrance of foreign organisms injures the quality of the final product. The vinegar-eel, a small nematode, is the bane of vinegar factories. Bacterial

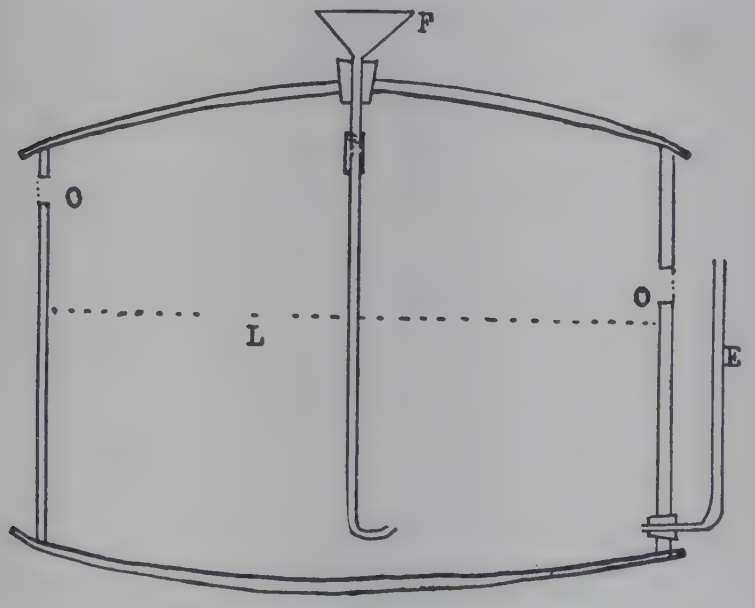


FIGURE 122

A vinegar barrel in cross-section. (After Conn and Conn.)

contaminations frequently cause putrid odours and cloudiness. Consequently, great care must be exercised in all stages of the manufacturing process. The type of fermentation utilized in the manufacture of vinegar has other commercial applications. Thus, acetic acid, apart from its presence in vinegar, was manufactured on a large scale during the war by fermentation, where heretofore it was made almost entirely from the destructive distillation of wood. Molasses and a seaweed called "kelp" (harvested in the Pacific Ocean) are the principal materials used in acetic-acid fermentation.

White lead (basic lead acetate), used extensively in paints of good quality, may be prepared by an acetic-acid type of fermentation. Grids of pure lead are piled between layers of

spent tan-bark. Acetic acid is developed during the fermentation of the bark and unites with the lead to form white lead.

Indigo, a valuable dye-stuff used in calico printing, like white lead, may be prepared either chemically or bacteriologically. Plants containing indican are placed in warm water, where fermentation proceeds. Indigo-white is formed. This is vigorously aerated, and so oxidized to indigo-blue, which is the indigo of commerce.

Acetone, an important ingredient in the manufacture of explosives, and butyl alcohol, another commercial solvent used for aeroplane "dope" or lacquer, were also manufactured extensively during the war, by the Fernbach process of fermenting corn and other cereals.

Lactic acid, of special value in the tanning industry, may be made from starchy substances, waste milk, or the whey from creameries, by fermentation with *Lactobacillus bulgaricus* in the presence of chalk. Even corn-cobs have recently been shown by Fred and Peterson to be a commercial source of lactic and acetic acids through fermentation.

Citric acid, normally present in lemons, may be prepared by the fermentation of various sugars by certain moulds.

Glycerine may likewise be named among the important organic compounds which may be made through the process of fermentation.

2. BREAD

Since the art of bread-making is so dependent upon yeast, it may be well to consider compressed yeast for a moment. Judging from the final product, one would never suspect that compressed yeast is made in much the same way that beer is brewed. Barley or rye "malt" is crushed, and a "mash" is made, which is inoculated with some vigorous lactic-acid-forming organisms, such as *Bacillus delbrücki*. The starch originally present on the cereal is thus converted into sugar. The filtrate or "wort" is used as a medium in which to grow the pure selected yeast culture, which is the "starter." Within twenty-four hours yeast growth has reached significant proportions. The yeast (often allowed to settle) and fermented liquid are put through continuous centrifuges and filter-presses to drain off the excess liquid. The result-

ing pasty mass of yeast forming the filter-press cakes is usually reinforced with a little starch or vegetable oil, which gives the yeast a better texture. The yeast is then moulded and cut into cakes of suitable size and shape. The latter are wrapped in foil in order that they may retain their moisture and are kept in cold storage; otherwise they would spoil by liquefaction. If the entire manufacturing process is not carefully controlled, contamination may result in a slimy or unpalatable product. Breweries and distilleries produce considerable yeast as a by-product, but this is unsuitable for human consumption since it retains the bitter flavour of hop resins. It may be utilized, how-

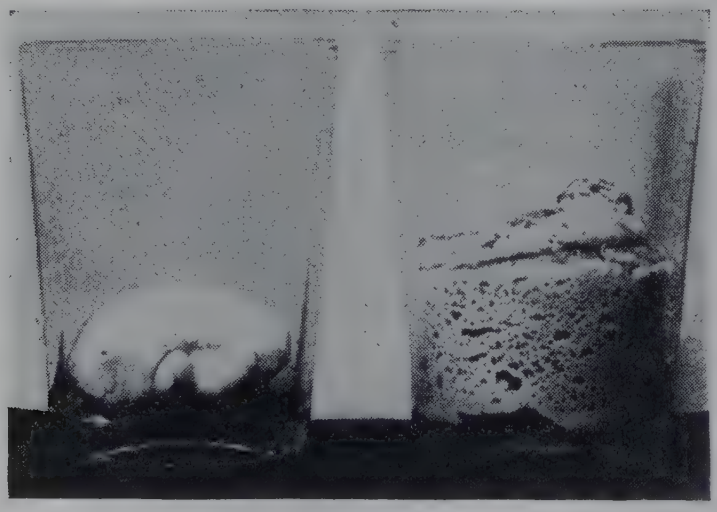


FIGURE 123

Samples of dough incubated overnight. At the left, without yeast; at the right, with yeast. (After Conn and Conn.)

ever, as food for cattle, or fertilizer. Yeast is rich in proteins and vitamin B. Many therapeutic claims have been made for yeast, but most of the virtues with which it is supposedly endowed have yet to be satisfactorily demonstrated.

The value of yeast in bread-making, however, remains unchallenged. (See fig. 123.) In most bakeries yeast, flour, water, salt, sugar (or some substitute), and shortening (fat or oil) are mixed at once and allowed to rise. This is known as the "straight-off" method. The housewife uses the "sponge" or "batter" method, in which a thin batter of yeast, flour, and other ingredients is mixed the day before the dough is made. "Sour dough" breads are commonly made in France and Italy, by permitting the development of lactic-acid bacteria, which impart a

characteristic flavour. The manufacture of bread requires much care in manipulation, particularly as regards mixing and control of temperature during rising and baking. Stale yeast or bacterial contamination causes the bread to have a yeasty or unpleasant odour, sour or soggy taste, or ropy texture. Is it not noteworthy that microbes are of such importance not only in the deterioration of milk, "the perfect food," but in the production of the "staff of life"?

3. FOODS PRESERVED BY FERMENTATION

Microbial activity in milk is not always undesirable, as we have seen in the preparation of sour-milk beverages and cheese. There are other fermented foods as well which have gained popularity. Among these may be mentioned sauerkraut, which is prepared by slicing cabbage, adding salt, and applying pressure to extract the juice. Fermentation takes place vigorously in the juice, the sugars being changed to acids (lactic, acetic, etc.). A certain amount of decomposition of protein occurs, which in the absence of salt would be putrefactive. The ready access of air must be avoided, since it would result in the introduction of moulds, which would "devour" the lactic acid. Other greens may be preserved in the same manner as sauerkraut by stimulating the lactic-acid microbes and checking putrefactive varieties.

Similarly, in the manufacture of pickles before vinegar or other condiments are finally added, a lactic-acid fermentation is encouraged by placing the cucumbers, cauliflowers, or other vegetables in brine of high salt concentration. The cucumbers may be allowed to remain in this fermenting-fluid for a year or more. "Subsequent pickling operations consist in leaching out the excess salt in warm or hot water, firming the flesh with a dilute solution of alum and impregnation of the cucumbers with plain or spiced or sweetened vinegar. Dill pickles are prepared by fermentation of cucumbers in a 40° to 45° brine (10 to 12 per cent sodium chloride salt) in closed barrels fitted with small vent holes for escape of gas. Dill and other herbs and spices are packed in the brine with the cucumbers before fermentation. Enough acid is formed to preserve the pickles

indefinitely if air is excluded. Often the finished pickles are pasteurized in lacquered cans for domestic use. The high acidity renders the sterilization very easily accomplished. . . . If vegetables of any variety are mixed with 25 to 33 per cent of their weight of salt they may be preserved indefinitely without fermentation, provided they are sealed in barrels or jars of moisture. Corn and string beans are excellent so preserved. The process offers a home method of preserving vegetables without danger from botulism. Where dry salt cannot be employed the vegetables may be packed in a saturated solution of salt. The salt preserved products must be soaked in water before use to remove excess of sodium chloride" (Marshall).

It is not commonly known that the green olive as sold today is a fermented product preserved by the lactic acid formed in the pickling process to which it is subjected. Green olives are treated with lye (about two per cent sodium hydroxide) in order to remove the bitter taste which the natural fruit possesses. The lye is then completely leached out of the olives with frequent changes of cold water. The olives are put in barrels filled with brine, which are placed in a warm room or in the sun. Spontaneous fermentation favouring the growth of lactic-acid bacteria occurs. The characteristic flavour of olives depends upon this fermentation process. Again, the salt in the brine inhibits the growth of undesirable microbes during the fermentation process, which lasts from six weeks to two months. Unless air is excluded, microbes will develop which destroy lactic acid, and the olives will become brown as a result of oxidation. Olives are packed in glass bottles without further sterilization, for the acidity developed in the manufacturing process acts as a preservative. Contaminating organisms cause spoiling and result in softening of the olives and the development of disagreeable flavours and odours. Cruess found *Bacillus coli* a common offender in this respect. He believes that a much more healthful and sanitary product would be obtained if bottled olives were pasteurized and there can be little doubt as to the wisdom of his recommendation.

"Ripe" olives are not tree-ripened fruit. They are even less like the natural fruit than green olives, for their colouring is *entirely* due to the treatment they receive rather than to the fact that

more mature olives are used. In general, in the manufacture of "ripe" olives, which are naturally green in colour, the fruit is placed in brine and allowed to ferment for about two weeks. The olives are then treated with lye solution long enough for it to penetrate somewhat below the skin. Following this treatment they are exposed to the atmosphere or to a jet of compressed air. In the presence of sodium hydroxide, present in the lye solution, and air, the olives become black. Hence the name "ripe" or "black olive." A second lye treatment follows, this time long enough to penetrate through the flesh to the pit. Finally, as in the manufacture of green olives, the lye is leached out with water. The "ripe" olive is usually canned or bottled in salt solution and sterilized. Heretofore there have been outbreaks of botulism due to imperfectly canned olives, green and "ripe," but effective methods have now been established which protect the public from such dangers.

Some foods are preserved by the process of fermentation, while others, on the contrary, suffer greatly as a result of fermentation. The latter fact has been referred to repeatedly, but there is one example which has a special interest — namely, the deterioration of cane sugar.

Most microbes have just as sweet a tooth as human beings. The consequent loss of cane sugar in storage runs into millions of dollars. Sugar, unless it is dry, as is refined sugar, is likely to have a film of moisture around each particle. This may be readily observed in raw, or brown, sugar, which has a coating of molasses. Bacteria moulds and even yeasts can thrive in this film. The microbes then attack the cane sugar, transforming it into a non-sweetening sugar. Such a chemical change is only roughly discerned, if at all, by the palate, but may be easily demonstrated by the polariscope, an apparatus which measures the purity of sugar very accurately. Large amounts of sugar, as purchased by the refineries in the United States, are paid for strictly on polariscopic test, so that the loss of any sweetening power in transport from Cuba or any other country where sugar-cane is grown extensively, or in storage pending the refining process, represents a considerable economic loss. The factors which make for the deterioration of sugar and their control have proved an interesting subject for research, the

results of which the author has already published.[1] It has been shown that moulds are particularly active in spoiling most of the unrefined sugars. A practical method for the elimination of moulds was suggested — namely, that of washing sugar in the centrifugals by superheated steam instead of water. The steam kills the moulds and at the same time produces a lighter-coloured sugar.

4. SPECIAL FERMENTATION PROCESSES

Although it is not generally known, fermentation is of value to the tobacco industry during the curing process. When the tobacco leaves are gathered, they are allowed to dry, after which they are cured by being piled in masses or packed in boxes, much in the same way that silage is made (as will presently be described). During the curing process the tobacco leaves may be moistened with water, sugar solutions, or aromatic substances to improve their flavour. Fermentation progresses with a production of heat. The nicotine, sugar, and water content decrease, while ammonia increases. Striking changes, which are highly desirable, occur in texture and flavour and colour. The final dark-brown colour and flavour of the tobacco are therefore due to the fermentation process.

In the curing of black tea, there is a similar fermentation, due to mould, rather than to bacterial activity. The tannic acid, which is the harmful principle in tea, is converted by this process into gallic acid. If too much moisture is present or the fermentation proceeds for too long a time, the tea may be spoiled by slime-forming bacteria.

In the curing of tobacco, tea, or other plants the enzymes secreted by the microbes are responsible for the conversion of one substance into another in the fermentation process. In the production of enzymes for medicinal purposes moulds themselves are used, as, for example, in *taka-diastase*, which is a diastase prepared according to the Takamine process. Diastase is the enzyme which breaks down starches into sugars.

Leather-manufacturers have successfully harnessed bacteria to their industry. Thus, when hides and skins are received at

[1] N. Kopeloff, *et. al.*: Louisiana Sugar Experiment Station *Bulletins* 166, 170, and 175

the tannery, there is usually a considerable amount of hair and flesh attached. This is "soaked off" in a lime solution. If the solution is not renewed frequently or an antiseptic used, bacteria multiply to such an extent as to make it putrid and injure the hides. At any rate, thanks to bacterial activity and soaking, the hair and flesh may be easily scraped off. Heavy, or sole, leather is then transferred to a dilute acid bath to remove the excess lime.

But soft leathers, such as are used for gloves, receive a treatment which may appear somewhat startling. The skins are placed in a dilute infusion of dog, pigeon, or hen dung in which bacteria have multiplied extensively. This fermentation process is known as "bating" or "puering." Such treatment makes the skin soft and pliable, but if prolonged unduly, the hide may become pitted or even dissolve to a considerable extent. (In recent times some successful efforts have been made to replace the dung infusions by chemicals and gland extracts.) The skins are then "pickled" in sulphuric acid and sodium chloride (table salt) to remove the lime added during "bating." Next the skins, ready for tanning, are placed in the tan pits, where tannin extracted from tan-bark penetrates the skins. Here again bacteria are active, particularly those of the lactic-acid type.

Similarly, linen and hemp are made by the *retting* of hemp and flax plants. The fibres of these plants are firmly bound together by a glue-like substance known as "pectin." The removal of pectin is therefore imperative before the fibres can be utilized. This is accomplished by the microbial activity of such organisms as *Bacillus amylobacter*, *Granulobacter pectinovorum*, or various moulds during alternate wetting and drying of the plants or during their immersion in water. After retting, the fibres may be easily separated, combed out, and used in spinning and weaving.

In coffee manufacture, too, fermentation plays an important initial rôle. It is fully as necessary to remove the outer covering of the coffee seed or "bean" as it is to remove the hair from hides prior to tanning. The pulp is removed from the matured coffee seeds after they have been picked and bagged, and the pulp and seeds are separated by flotation in water. The depulped seeds are then allowed to ferment in order to remove

the outer parchment and silver lining, on the same principles as are employed in the retting of flax. The seeds are dried after fermentation and run through a peeling-machine which removes the enveloping tissues. The coffee seed is then ready for roasting.

Cocoa, like tea, contains a bitter principle which may be considerably reduced by fermentation. Cocoa beans are scrubbed and dried after they have been gathered. They are then subjected to a fermentation process which aids in the removal of the outer covering, just as in the manufacture of coffee. Yeasts are instrumental in this fermentation, which results first in the formation of alcohol. The oxidation of the tannin of the cocoa bean determines its taste, aroma, and brown colour fully as much as the roasting, to which it is finally subjected.

Soy-bean sauce, rarely known by that name, is the dark-brown fluid which is used to season chop suey. It is also the principal ingredient of many dark-brown sauces which are marketed at a fancy price for the purpose of seasoning meats, fish, etc., at the table. Soy-bean sauce is prepared by cooking soy-beans and mixing them with prepared wheat. The mass is then inoculated with a mould (an *Aspergillus*), so that fermentation may proceed. A mash is made by emptying the above mixture into strong brine. The mash is aerated and stirred. Then the thick, dark-brown mash is pressed, or the fluid siphoned off. This is the soy-bean sauce, which is finally filtered and boiled or pasteurized. It is important in this process to prevent the development of bacteria, since the latter impair the flavour of the final product.

Not only is fermentation important in the manufacture of food for human beings, but it also finds a place in the production of food for cattle known as silage. Silage bears a close resemblance to sauerkraut in that it consists of greens which have been allowed to ferment, with a production of lactic acid. The whole corn plant is generally used, alone or in combination with pea-vines, hay, etc. The material is chopped into small pieces and packed into a silo, which is a tall, air-tight compartment. Since the harvested plants contain an ample supply of starches, sugars, and moisture, the microbes flourish and fermentation occurs. Recently the attempt has been made to add a "starter"

of *L. bulgaricus* to ensure lactic-acid fermentation. Other undesirable types of fermentation may initiate putrefactive processes which result in a malodourous and unpalatable silage — even in a product which may poison cattle (as when *Bacillus botulinus* is present).

Fermentation, properly controlled, is of indubitable value in industry. From the long list of instances in which it is applied, a few of the principal ones have been selected, dealing with the preparation and preservation of food, condiments, and beverages. Undoubtedly the future holds in store many more fermention processes which will add further to our enjoyment of life.

Chapter XXX

MONEY AS A CARRIER OF MICROBES

Not only the industries which harness microbes, but all industry and commerce has money as its paramount consideration. Money is continually in circulation — all of us come in contact with it daily. We know that disease may be transmitted by contact, yet who pays any attention to this important individual and public-health problem? One unhesitatingly pays a penny for a drinking-cup, but rarely gives a thought to the germs carried by the penny itself. It is a well-known fact, however, that lesions of the skin, even those which are invisible, are the favoured portal of entry for the microbes responsible for such diseases as anthrax, lockjaw, gonorrhœa, and syphilis. There are, besides, a host of others that enter through the respiratory tract: pneumonia, diphtheria, influenza, and the like.

Money, passing as it does through the hands and pockets of many individuals with great frequency, has an exceptional opportunity of becoming a carrier of disease. Some banks, realizing the possible danger involved, have made it a practice to provide disinfectants for their employees. Certainly if the banks consider this a wise precaution, it deserves more than passing notice from the man in the street. It has been repeatedly proved that infection may readily result from handling contaminated material. Thus, in an interesting study of the bacteria to be found on postage stamps it was shown by Keilty and McMaster, several years ago, that out of fifty stamps examined all but two had bacteria upon them. They state that it is dangerous to lick stamps, since they are laden with bacteria which might belong to the types that produce disease. For those who indiscriminately lick stamps, this should carry a convincing message.

As far as the public is concerned, postage stamps and money have much in common, although they differ considerably in composition. Coins which are infected carry living bacteria for a

short time after infection, as shown by Park. He took coins from children having diphtheria and tested them for living bacteria six hours later. Out of thirty-five pennies, three had living diphtheria bacilli. He happened to be primarily interested in money handled by persons known to be infected. But it is well to bear in mind that many individuals who are in good health also have the unfortunate faculty of distributing typhoid and diphtheria bacilli *ad infinitum*. Such persons, known as "carriers," constitute one of the chief problems of public-health hygiene.

Paper money carries large numbers of bacteria. The average count of bacteria on bills has been estimated at 142,000. While it is very difficult to prove that the bill is the actual agent in transmission of disease, it is nevertheless logical to suppose that passing a platter of 142,000 microbes from hand to hand will result in someone's getting a helping. There is a marked difference in the number of bacteria found on different kinds of paper money. Old bills are laden with great numbers of organisms, while new bills contain only a few bacteria.

The actual numbers and types of bacteria to be found on subsidiary coins and currency in general circulation are perhaps of even more interest than those on bills, because they are handled with greater frequency. The majority of bacteria found on coins are said to belong to the type which can go into the "spore" or resting state. This makes it possible for them to persist for long periods of time and reproduce at the first favourable opportunity. The number of bacteria on coins has been found to vary between 0 and 2950.

Fortunately, the metallic composition of the coin acts in a bactericidal manner. That is, metals such as copper and nickel have the power to kill microbes. Yet such coins may carry certain types of bacteria that defy the germicidal properties of the metals used in making coins.

While there is some reassuring information concerning coins, it does not hold for paper money, which contains no metals capable of destroying bacteria. There is certainly no justification for the unsanitary practice of placing money in the mouth, whether it be by parent or child, and of wetting the finger in the mouth while counting bills. No one would refuse money on

the basis of its bacterial count, but there should be some realization of the rôle which money can play in the spread of disease.

Microbes, harmful and harmless, are all about us. Many of the harmless ones, as we have observed, have been turned to man's advantage. Against the harmful ones we must wage continual warfare in an effort to destroy them. Let us, then, inquire into the methods whereby microbes can be destroyed.

Chapter XXXI

DISINFECTANTS AND THEIR VALUE

Bacteriology has been a great boon to civilization — and an awful nuisance. No one will deny that the knowledge of bacteria has preserved health and prolonged life, yet everyone will admit that it has interfered with personal pleasures. Bacteria tyrannize over your daily existence. You leave your warm bed to shiver in the morning chill because you must leave your bedroom window open at top and bottom at night. Then starts the daily round of self-flagellation, beginning with the blood-letting bristles of the tooth-brush and ending with the same. Soap intended for cleansing is sure to get into your eyes. You worry over the well-advertised diseases you will acquire if you do not use this tooth-paste or that soap. You spend twenty minutes puttering and yawning over the sterilization of the baby's bottles. Yet you must not kiss the baby on the mouth. You break your finger-nail on the pasteurized milk-bottle; you gag at the chlorine that sterilizes your drinking-water, and you wrestle with the waxed paper on the bread. Your daily habits are dictated by the Commissioner of Health. You must keep step in the fight against bacteria, or his statistics will suffer. In a word, you pay the premium of personal hygiene on the life insurance of the community.

It was not ever thus. The cave-man never hesitated about kissing his neighbour's wife because he might bring home influenza. His hearty sneeze aroused admiration and not outraged glances. He grew a barbarous beard and never heard of the germ of lockjaw that lurks in the soil. When this germ entered a spear wound, he was cursed with a horrible death — not saved for another war by an antitoxin injection.

Even today many a housewife prefers to harbour a few bacteria rather than asphyxiate her family with some evil-smelling disinfectant. As everyone knows, a disinfectant is a chemical agent which destroys harmful microbes.

The number of disinfectants now on the market is enormous and the intelligent choice of any single one depends upon several factors, foremost among which are efficiency and uniformity. Thus, a loosely corked bottle of peroxide of hydrogen is as ineffectual as a bottle of champagne from which the bubbles have escaped. Consider, too, the effect of the disinfectant upon the substance to be disinfected. One would not ordinarily disinfect a Persian rug with tincture of iodine. Other factors to be kept in mind in choosing a disinfectant are its facility of use and its cost, the most expensive disinfectant not being necessarily the best for all purposes. It is no exaggeration to say that most of the patent disinfectants are more expensive than they should be. The public pays for the advertising, not for the ingredients, which, as a rule, are not disclosed to the gullible purchaser, who buys merely an attractive trade-mark.

The relative efficiency of different disinfectants is difficult to establish. Examine the various labels. They bear glowing accounts of the countless benefits to be derived from the use of such and so. They even give you the phenol coefficient. But what does it all mean? What is one to look for in purchasing a disinfectant and what considerations should determine one's choice? Obviously, the cost is a primary consideration. But the consumer willingly pays a higher price for a superior article. The purpose for which any disinfectant is intended, facility in application, and uniformity of manufacture are also important. These the consumer may judge for himself. But he must rely on a laboratory to supply fundamental data concerning the disinfectant, its strength (concentration), the liquid in which it is dissolved, the time required for the disinfectant to kill, and, finally, the kind and number of bacteria to be killed.

First, consider the nature and strength of the disinfectant. One does not ordinarily think of common table-salt as an antiseptic. But it is. One part of table salt in six parts of water will prevent the growth of most bacteria. Table salt, known to chemistry as sodium chloride, is feeble, however, in its action upon bacteria when compared with other chemical substances, such as carbolic acid (phenol). For one part of carbolic acid dissolved in 333 parts of water is as effective as one part of table salt in 6 parts of water. In other words, carbolic acid is as potent

as table salt in fifty times as much water. Roughly speaking, a pinch of carbolic acid in about a quart of water would kill as many microbes as a pinch of table salt in a teaspoonful of water. Pure carbolic acid consists of colourless crystals, which are so powerful as to raise blisters if the skin touches it — therefore, a "pinch" is to be taken any way but literally. The stronger the disinfectant, the more it can be diluted and still prove effective, although the efficiency of any disinfectant is reduced by dilution beyond a certain point. For example, a pinch of carbolic in a quart of water will kill many harmful microbes, but if the amount of water be doubled to two quarts, then most of the harmful microbes, though inhibited in their power to grow, will not necessarily be killed. In the first instance the solution is a disinfectant, in the second an antiseptic.

A certain distinction, therefore, is drawn between disinfectants and antiseptics. A disinfectant kills harmful microbes or injures them to such an extent that they will not grow even if offered the most favourable environment. An antiseptic hinders or prevents the growth of microbes, although it does not necessarily kill them. The two terms are loosely and interchangeably used through either ignorance or carelessness. Still another common misconception attaches to "germicide." A germicide is a substance which *destroys all* microbes. It differs from a disinfectant in that the latter, though it kills all *harmful* microbes, may not necessarily kill all harmless ones.

It is evident that a single substance may act as an antiseptic, as a disinfectant, or as a germicide. To illustrate: 1 part of carbolic acid in 1000 parts of water acts as an antiseptic. But to act as a disinfectant, 10 parts of carbolic acid should be placed in 1000 parts of water. In order to kill the spores (the resistant, resting stage) of bacteria, about 50 parts of carbolic acid to 1000 parts of water are required. The inference to be drawn from this example is that many substances may be strong enough to act as antiseptics in preventing bacterial growth, but are not powerful enough to be germicides. In choosing either an antiseptic or a germicide the purpose for which it is intended must be clearly borne in mind. Thus, you wouldn't use a lavatory disinfectant for gargling your throat.

In judging the efficiency of any disinfectant the nature of

the liquid in which it is dissolved is highly important. Nitrate of silver, for example, dissolved in pure water is not so effective as nitrate of silver dissolved in a mixture of three parts of water and one part of alcohol. This may be accounted for by the penetrating power of the alcohol, which permits the nitrate of silver to get deeper into the tissues than it would otherwise.

The time required for a disinfectant to kill determines the strength or concentration to be used. Observe that carbolic acid in a dilution of one part of to ninety of water kills bacteria in five minutes, but if ten more parts of water are added, making a dilution of one part of carbolic acid to a hundred parts of water, twice this time is required.

A consideration of the nature of the microbe to be killed and the numbers in which it is present must enter into the choice of the method of disinfection to be used. Some kinds of bacteria are more easily killed than others. Thus, to kill spore-bearing rods and their spores, such as lockjaw (tetanus) bacilli, requires roughly five times as strong a disinfectant as to kill a non-spore-bearing streptococcus, which is a pus-forming spherical organism. Again, where the bacteria are multiplying rapidly in a deep wound, more frequent applications of disinfectants are required than where there are only a few bacteria present on the surface of the skin. Finally, the higher the temperature, the greater is the killing power of a disinfectant.

Effective advertising, as has been said, makes the public more familiar with the patented names of antiseptics than with their essential ingredients. The latter comprise a number of common chemicals of undoubted value. Let us briefly consider their relative merits, grouping them in the following order: inorganic disinfectants (without carbon); gaseous disinfectants; and organic disinfectants (containing carbon).

Doubtless the first chemical (inorganic) substance that comes to mind in thinking of disinfectants is bichloride of mercury, also known as corrosive sublimate. It is generally sold in tablets coloured blue so that they can be easily distinguished from aspirin or other non-injurious tablets. Despite this coloration one not infrequently reads newspaper accounts of someone who has gone to the drug cabinet at night for a headache cure and carelessly taken a blue tablet, only to awake in the hospital, if he is

lucky, with a much worse headache. A single tablet of bichloride of mercury usually contains more than twice the amount necessary to kill a human being, unless antidotes are promptly applied. Be doubly cautious and place your bichloride-of-mercury tablets on the topmost shelf of the medicine chest. It is a curious fact that opium-eaters are said to be able to take enormous doses without evil effect. White of egg — albumen — is effective in cases of mercury poisoning.

Bichloride of mercury has many uses, chiefly external. It is employed to disinfect the skin, whether of the hands or of the body. It has been used to treat wounds and for vaginal douches. But the latter practice is very dangerous, since it is now known that corrosive sublimate is an irritant to delicate tissues, and its prolonged application may cause chronic mercury poisoning. Syphilis, the venereal disease caused by a spirochæte, is frequently treated with corrosive sublimate. Never confuse corrosive sublimate with calomel, another mercury compound used to disinfect the intestinal tract, for death will be the price of your mistake. A solution of one part of bichloride of mercury to a thousand parts of water is recommended for external use; when this disinfectant is used to kill bacteria in organic materials, such as sputum, excreta, etc., less than five hundred parts of water should be employed, because a stronger solution is required. But since it tends to form inert compounds with organic materials, which usually contain albumen, bichloride of mercury is less efficient in dealing with them than are other disinfectants. The chief disadvantage of bichloride of mercury as a general disinfectant is that it corrodes metals; hence its name "corrosive" sublimate. It is also irritating to the human skin and unless it is combined with alcohol has little penetrating power.

Everyone who has had nitrate of silver applied to his tonsils knows what a caustic agent this chemical is. Yet it has only about one-quarter of the disinfecting power possessed by bichloride of mercury and loses its efficiency by combining with albuminous materials present in all human tissues. Nitrate of silver is usually employed as a surface antiseptic, but it has the disadvantage of leaving a black stain. The use of silver caustic in the treatment of epilepsy, St. Vitus's dance, and other nervous diseases has an ancient history. It dates from the period of

astrological medicine, practised by the Arabs, who taught that nervous diseases were especially affected by the phases of the moon, which were associated with silver in the human body, whence is derived the term "lunacy."

To anyone brought up on a farm, chloride of lime, or bleaching powder (chlorinated lime), is a familiar substance. But not everyone knows that it is made by passing chlorine gas over quicklime. Chloride of lime, therefore, has the strong characteristic odour of chlorine, a penetrating gas which was widely used during the World War. One part of chloride of lime when dissolved on one hundred parts of water forms an acid (hypochlorous) which kills most bacteria in from one to five minutes; one part in a hundred thousand parts of water will kill typhoid bacilli within twenty-four hours. Spores of bacteria can be killed by a five-per-cent solution in about one hour. As a dry powder, chloride of lime is useful in disinfecting excreta, yards, etc. It is a powerful deodorant. A deodorant may or may not be an antiseptic. Essentially it is merely a substance that absorbs odours. Any disinfecting value which a deodorant may have depends upon the character of its chemical constituents. Chloride of lime bleaches fabrics, but it also destroys them. It is likewise irritating to the skin. By special methods of preparation, however, as in Dakin's solution, this defect has been overcome. In using it for the treatment of wounds it is necessary to apply it at frequent intervals or by constant irrigation, since its power to kill microbes lasts for only a very short time. Again, Dakin has prepared organic chlorine compounds in oil, notably chloramine-T and dichloramine-T, which liberate the chlorine so slowly that their activity extends over a long period of time. When boric acid is added to chloride of lime, a non-irritating antiseptic is formed, called "eusol."

Among the cheapest disinfectants are lime combinations. Slaked lime, which is burned limestone to which water is added, when carefully stoppered from the air, is very effective at the rate of one pint of water to two pounds of burned lime (quicklime, calcium oxide). A three-per-cent solution of slaked lime, known as lime-water, will kill typhoid bacilli in one hour; a twenty-per-cent solution, when mixed in equal parts with infected fæces or other filth, will kill all the microbes present

within two hours. Upon exposure, slaked lime quickly absorbs carbon dioxide from the air to form precipitated chalk (calcium carbonate), a substance without any disinfecting value.

Until very recently no household would fail to have a vial of tincture of iodine. In seven-per-cent solution it is widely used as a skin antiseptic. Its chief disadvantage is that it stings in open cuts. It also causes discoloration. This is a cosmetic disadvantage, but a distinct asset in that it marks the site of application. Is it not reassuring to know that the antiseptic has been thoroughly applied? The colour not only aids as a reminder to keep the surface free from possible contamination, but serves as a bull's-eye for injections with a hypodermic needle. Trichloride of iodine, the combination of chlorine and iodine, is a powerful disinfectant, five parts to one thousand parts of water killing living bacteria, and ten parts to one hundred parts of water killing spores, within a few minutes.

One might suppose that acids are powerful germicides, but such is far from being the case. For example, one part of sulphuric or hydrochloric (sometimes called muriatic) acid to five hundred parts of water kills typhoid bacilli in one hour, whereas less than one-hundredth of this amount of bichloride of mercury will produce the same effect. But these mineral acids, sulphuric, and hydrochloric, are more effective than the vegetable acids, such as citric, present in lemons; malic, present in apples; etc. Boric acid, popular as an eye-wash, must be as strong as a two-per-cent solution to act as an antiseptic. Benzoic acid is also a weak antiseptic. It is used in preserving ketchups and foods of all kinds, as is benzoate of soda, against the use of which Dr. Wiley, in the interests of pure food, has fought so strenuously — and with justice.

The alkalis — sodium, potassium, or ammonium hydroxides — are more effective than acids. A one-per-cent solution of lye, or caustic soda (sodium hydroxide), for example, kills living bacteria in a few minutes. Spores are killed in less than an hour by a four-per-cent solution. Sodium carbonate in five-per-cent solution will kill living bacteria in a short time, but when heated almost to boiling will kill spores within ten minutes. This chemical is universally used in the sterilization of surgical instruments, hypodermic needles, etc., to prevent rusting after boiling.

Among the chemicals of more limited application are permanganate of potash (permanganate of potassium), the purplish-coloured antiseptic, which is slightly more effective than the alkalis just described. It is frequently used as a mouth-wash. Sulphate of copper, which is about one-half as powerful as bichloride of mercury, is especially valuable in killing algæ (the lowest forms of plant-life having green pigment) in the purification of drinking water. Chloride of zinc is a weaker disinfectant than sulphate of copper.

Having considered the inorganic chemical agents in common use as disinfectants, we may now turn our attention to the familiar gaseous disinfectants. The most widely used is undoubtedly peroxide of hydrogen, the notorious hair-bleach, which is also an energetic disinfectant because it releases nascent oxygen, the gas that bubbles away so merrily when this disinfectant is applied. Peroxide of hydrogen must be used with discrimination, for it loses much of its disinfecting power when in contact with blood or pus. Therefore the surface to which it is applied should be as free from organic matter as possible. One part of good commercial peroxide of hydrogen to two parts of water kills living bacteria; two parts of peroxide of hydrogen to one part of water kills spores. It should be noted, however, that many commercial hydrogen peroxides are so unsatisfactory as to have little if any disinfecting value.

The poison gas, chlorine, was a well-known disinfectant even before the World War. One part of chlorine gas to one million parts of water kills typhoid bacilli in a few hours and is therefore especially valuable in the purification of water-supplies. Most large cities use it to purify water because it is economical as well as efficient. As an antiseptic, two parts of chlorine to one thousand parts of water kill living bacteria almost immediately and spores within five minutes. Chlorine gas is not nearly so effective dry as when it is present in water, where it liberates nascent oxygen, making it similar in activity to peroxide of hydrogen.

Another gaseous disinfectant, also more effective in a moist than in a dry state, is sulphur dioxide, owing to its formation of sulphurous acid, which is not quite so potent a disinfectant as sulphuric or hydrochloric acid. Sulphur dioxide was formerly

widely used in the disinfection of all living-quarters, hospitals, ships, and wearing-apparel. Many experiments have established that exposure for eight hours or more to an atmosphere containing at least four volumes per cent of this gas in the presence of moisture will kill practically all disease-producing bacteria which do not form spores. "Four pounds of sulphur burned for each one thousand cubic feet [of space] will give an excess of gas" (Park and Williams).

Among the organic disinfectants there is one, formaldehyde, which is now generally regarded as the most satisfactory of gaseous disinfectants. For its proper use the room to be disinfected must be sealed tight with paper strips or cotton, the various articles of clothing etc., spread out, drawers and closets opened, and a supply of moisture provided. Anyone who has had occasion to use formaldehyde in any of its commercial forms knows its chief disadvantage — namely, its irritating effect on mucous membranes of the eyes, nose, and throat. On the other hand, it is an effective disinfectant, for a two-per-cent solution of formalin (which contains forty per cent of formaldehyde gas dissolved in water) kills living bacteria in less than a half-hour. It is, moreover, an excellent deodorant, for it forms true chemical combinations with putrefying substances, rendering them odourless. It has been used for preserving meat, milk, and other organic materials, although it is asserted by Trillat that it makes such products more indigestible. Formaldehyde solution (four per cent) is also used for preserving diseased tissues and brains for future microscopic study.

The word "antiseptic" for most of us has an olfactory association with carbolic acid (phenol). Carbolic acid "smells clean." Lister made it famous when he devised a special machine to spray the walls, dressings, etc., in his operating-room. Carbolic acid has a penetrating odour and a burning taste. It does not dissolve readily in water and should therefore be thoroughly mixed before using. "It is not destructive to fabrics, colors, metals or wood and does not combine as actively with albuminous matters as bichloride of mercury. It is therefore more suitable for the disinfection of feces, etc. A solution having one part [of carbolic acid] to one thousand [parts of water] inhibits the growth of bacteria; one part to four hundred kills the less re-

sistant bacteria; and one part to one hundred kills the remainder. A five per cent solution kills the less resistant spores within a few hours and the more resistant in from one day to four weeks" (Park and Williams). Warming carbolic acid increases its destructive action. In combination with alcohol, unlike bichloride of mercury, it loses much of its disinfecting power.

Carbolic acid, as we know it, is a chemically pure substance. The principal ingredient of the so-called crude carbolic acid is cresol, which has true disinfecting properties. It is practically insoluble in water; consequently its usefulness is limited. Many methods are employed to bring cresol into solution, so that its powerful disinfecting properties may be utilized. A refined mixture of the three cresols present in crude carbolic acid is tricresol. It is only very slightly soluble in water, but its disinfecting power is about three times as great as that of pure carbolic acid. "Lysol" contains about fifty per cent of cresols. It mixes readily with water to yield a clear, soapy liquid, and its germicidal action is slightly superior to that of pure carbolic acid. Creolin is an emulsion of cresol and rosin soap.

The destructive distillation of pine-wood yields tar. It is used as a skin antiseptic and as an "expectorant" in cough mixtures. It is a cheap but valuable disinfectant for excreta, etc., where even crude carbolic acid might be considered expensive. When wood-tar is subjected to further destructive distillation, creosote is formed. One part of creosote to two hundred parts of water kills many bacteria in ten minutes, but fails to kill tubercle bacilli in twelve hours. Creosote formerly was a popular ingredient of cough mixtures but the medical profession now prefers to treat tubercular and other lung affections by general hygienic measures rather than by drugs.

Contrary to common belief, alcohol is a rather poor disinfectant for external purposes. Curiously, equal parts of alcohol and water are more effective than pure alcohol. Strong as well as weak concentrations are not particularly destructive to bacteria. A fifty-per-cent solution of alcohol will kill living bacteria within fifteen minutes. A moderate amount of alcohol does much to enhance the efficiency of corrosive sublimate, but diminishes the value of carbolic acid, formaldehyde, etc.

One of the best illustrations of a chemical which has a

powerful odour, but weak antiseptic properties is iodoform. At one time it had considerable vogue, particularly in surgical conditions. Iodoform liberates iodine, which not only combines with poisons already formed by bacteria, but also exercises a destructive action upon them. Reminiscent of operations, too, is the sickeningly sweet odour of chloroform. In a one-per-cent solution it kills bacteria, but not spores. Chloroform is used in the laboratory as an antiseptic in keeping down microbial growth in blood or antitoxic serums.

Fast coming into popularity so great as to rival tincture of iodine is mercurochrome, which is a red dye containing mercury. It can be used internally as well as externally. Mercurochrome bids fair to replace tincture of iodine because it does not sting in open wounds, and, further, it does not have the irritating effect of bichloride of mercury. Moreover, it appears to be valuable in treating blood-poisoning, kidney, and other infections. As an ordinary external antiseptic, however, many authorities question whether it is as effective as tincture of iodine. Other brownish-red dyes are those belonging to the flavine series: flavine, proflavine, and acriflavine. These were effectively used in treating wounds during the World War. Still other dyes, including gentian-violet, malachite-green, and brilliant green, have also proved of great antiseptic value.

Silver preparations other than silver nitrate and less powerful in killing bacteria are argyrol, protargol, and collargol. They do not possess the irritating properties of silver nitrate and therefore have been extensively employed in the attempted disinfection of the mucous membranes. Silver preparations should not be used continuously for long periods, as poisoning is likely to result.

There is little point in enumerating all the substances possessing disinfecting value, for the list is overwhelming. Nor is this the place for a discussion of patented disinfectants, because on the one hand there is the danger of being accused of holding a brief for some particular product and on the other of being sued for libel. The interested reader who desires an impartial verdict will do well to consult *New and Non-Official Remedies*, an authorized publication of the American Medical Association.

For purposes of standardization all antiseptics or disinfect-

ants are arbitrarily compared with carbolic acid. By actual test it can be definitely stated exactly how many times stronger or weaker than carbolic acid is the disinfectant under investigation. The result is known as "the carbolic acid (phenol) coefficient." The Rideal-Walker method of standardizing disinfectants as modified by Anderson and McClintic is the method employed by the United States Public Health Service.

The principles upon which it depends are as follows: Various dilutions of pure carbolic acid are made so that the series includes one strong enough to kill the test organism, *Bacillus typhosus* (causing typhoid fever), in two and a half minutes; and one weak enough to fail to kill the bacteria in fifteen minutes. There are, in addition, a large number of intermediate dilutions. The disinfectant to be tested is also variously diluted. The same numbers of bacilli are seeded into the different dilutions of the disinfectant and exposed for varying periods of time. Immediately thereafter the various dilutions are subcultured to determine whether the bacilli are dead or alive, and the number of minutes required to kill them is thus established. The following example, taken from Zinsser, is frequently cited:

1 *Sample*	2 *Dilution*	3	4	5	6	7	8	9 *Phenol Coefficient*
		Time of Exposure						
		2.5	*5*	*7.5*	*10*	*12.5*	*15*	
Phenol (Carbolic Acid)	1 to 80	−	−	−	−	−	−	
	1 to 90	+	−	−	−	−	−	
	1 to 100	+	+	+	−	−	−	
	1 to 110	+	+	+	+	+	−	$\frac{375}{80} = 4.69$
Disinfectant A	1 to 350	−	−	−	−	−	−	$\frac{650}{110} = 5.91$
	1 to 375	−	−	−	−	−	−	
	1 to 400	+	−	−	−	−	−	$2)\ 10.60$
	1 to 425	+	+	−	−	−	−	$5.30 =$
	1 to 450	+	+	−	−	−	−	Coefficient
	1 to 500	+	+	−	−	−	−	
	1 to 550	+	+	+	−	−	−	
	1 to 600	+	+	+	+	−	−	
	1 to 650	+	+	+	+	+	−	
	1 to 700	+	+	+	+	+	+	
	1 to 750	+	+	+	+	+	+	

The above chart is easily explained. In column 1 are listed the samples: first, the standard carbolic-acid solution; secondly, the Disinfectant A to be tested. In column 2 are recorded the dilutions as expressed in parts of disinfectant to parts of water — i.e., 1 to 80, means one part of carbolic acid to eighty parts of water. In columns 3 to 8 are given the number of minutes during which the test organism is exposed to the different dilutions of carbolic acid and Disinfectant A. The minus sign (−) indicates that the bacteria have been killed, the plus sign (+) means that they have survived the exposure. To determine the carbolic acid coefficient the weakest dilution of Disinfectant A which kills the test organism in 2.5 minutes is divided by the weakest dilution of carbolic acid which kills the test organism in 2.5 minutes. In the above chart it will be seen that the weakest dilution of carbolic acid which kills in 2.5 minutes is 80, because in 1 to 90 there are living bacilli. The weakest dilution of Disinfectant A which kills in 2.5 minutes is 1 to 375, because at 1 to 400 there are living bacilli. Dividing 375 by 80 gives 4.69. The same method is used for calculating the weakest strength which kills in 15 minutes; for Disinfectant A this is 650, for carbolic acid 110. Dividing 650 by 110 yields a quotient of 5.91. The two values 4.69 obtained for 2.5 minutes and 5.91 for 15 minutes are averaged (add and divide by 2) yielding a final carbolic-acid coefficient of 5.30. In other words, Disinfectant A is 5.30 times as strong as carbolic acid, as is evidenced by its power to kill the test organism when more water is present. Obviously, the stronger the disinfectant, the more water can be added to it without impairing its ability to kill bacteria. Antiseptic strength, or what is termed the "coefficient inhibition" — namely, the strength of chemical necessary to prevent bacterial growth without necessarily killing all the bacteria — is determined in a somewhat similar manner.

In this connexion it is of interest to quote from a recent editorial of the *Journal* of the American Medical Association: "While physicians understand that a germicide may produce effects on an infected area in a brief period which can be produced by an antiseptic only through prolonged contact, the general public understands these terms as synonymous. In consideration of this condition, the U. S. Bureau of Chemistry,

which is charged with the enforcement of the Food and Drugs Act, has recently come to the conclusion that the term 'antiseptic' when used in the labelling of a medicinal product is objectionable unless the preparation when used as directed will actually destroy micro-organisms. In considering the wording of a drug label, the bureau holds in consonance with court decisions that the language used is to be given the meaning ordinarily conveyed by it to those to whom it is addressed. Since an antiseptic remedy means to the public one that acts against sepsis — that is, prevents the condition as much as possible — the bureau holds that the purchaser of such a preparation should therefore be given full benefit of this meaning of the term. If this is not done, a false sense of security is produced and possibly valuable time wasted in using a product that does not have positive germicidal effect. This is especially true of such products as mouth washes, sprays, gargles and douches, which are widely advertised to the public. These preparations are necessarily in but brief contact when administered and are subject to immediate dilution *in situ*. If, therefore, the effect produced involves only inhibition, their action on micro-organisms must be inconsequential." [1]

The practical application of disinfectants is of utmost importance. It should be realized that disinfectants are only an aid in protection against disease: they can never be all-sufficient. Cleanliness is essential, as are sunlight and pure air. As Park, Williams, and Krumwiede aptly say: "Practical disinfection never affords complete protection; and perfect cleanliness is better, even in the presence of contagious disease, than filth with disinfection, as it is ordinarily carried out." The proper washing of hands and body will do much to prevent bacterial contamination. Special soaps, particularly those of high price, are usually unnecessary luxuries, for price bears little or no relation to the benefit of soap-suds. Frequency of laving is the important consideration. Boiling kills most microbes; therefore it is important that food and drink which harbour microbes should be thoroughly cooked.

The large variety of needs to which antiseptics and disinfectants are applied is somewhat bewildering. Having considered

[1] *Journal* of the American Medical Association, LXXXVIII (1927), 1420–1.

the relative merits of those in common use it might be well to survey, as does Cushny, the general principles underlying the treatment of various infections:

In surgery today, disinfectants are not used as generously as they were by Lister, who believed that it was not enough to treat infected wounds with disinfectants, but that the infection of wounds could be avoided by the use of antiseptics which prevent the growth of microbes. The present conception, however, is that a clean wound needs no antiseptics and will heal more rapidly if none are applied. Disinfection in surgery is now limited to tissues already infected and to objects which are likely to come in contact with a clean wound. The skin of the patient and of the surgeon are most difficult to sterilize and a variety of drugs have been used for this purpose. Those most commonly employed to disinfect the skin or to kill the microbes in a wound already infected are bichloride of mercury, hydrogen peroxide, tincture of iodine, mercurochrome, etc. Drugs should not be too lavishly used in dressing wounds. Poisoning may result, as it does sometimes when powerful disinfectants are used to wash out organs such as the uterus. In the treatment of skin disease, however, disinfectants may be used more freely. Among the milder remedies are pyrogallol, chrysarobin, naphthol, resorcin, and members of the tar series. More powerful chemicals may be employed if only a restricted portion of the skin is to be treated.

In treating respiratory infections it is hard to find antiseptics which are sufficiently powerful to destroy microbes without damaging the tissues. The same predicament is encountered in attempting to disinfect the intestine. Creosote and other members of the tar series have been extensively used for respiratory infections. Most of the skin disinfectants are too powerful to introduce into the intestine, but some of the cresols have been used. Salol, which is harmless in the stomach (to the patient), becomes active against bacteria in the intestine. Purgatives, such as calomel, are chiefly to be recommended. Infections in other internal organs are almost impossible to treat satisfactorily. Nor can we ordinarily destroy disease-producing microbes that are lodged in the tissues. True, some internal diseases have been successfully treated, as, for example, malaria by quinine, syphilis by such arsenicals as "606," etc.

Again, finding a suitable antiseptic which will not irritate the delicate membranes is the difficulty in the treatment of genito-urinary infections. Urotropine and, more recently, mercurochrome and hexyl-resorcinol have been reported to yield good results. In catheterization, silver-nitrate solution is used as a safeguard against infection.

The care of the sick-room, particularly in the presence of such contagious diseases as measles, scarlet fever, diphtheria, tuberculosis, etc., requires the frequent use of disinfectants, not only for those attending the patient, but for the soiled clothing, towels, napkins, bedding, eating-utensils and discharges as well. Carbolic acid serves most purposes well. The addition of common washing-soda to hot soap-suds is an economical and efficient method to be recommended for cleansing purposes. The fewer articles in the sick-room, the better; consequently it is advisable to remove carpets, curtains, and superfluous upholstered furniture.

The microbes of disease pass readily from one human being to another. Disinfectants often give a false sense of security. In general, microbes on the surface of the body or other objects are more easily killed than those in the mucous membranes of the eye, nose, and throat. Antiseptics which are strong enough to kill bacteria in those passages are likely to prove very irritating and thus do more harm than good.[1] Antiseptics and disinfectants should be employed, however, whenever practicable, to prevent the dissemination of microbes. This principle is of special importance in disinfecting the surroundings of patients who have recovered from or died of infectious diseases.

Disinfection is our watchword, and disinfectants are our weapons of defence against disease-producing microbes. The arsenal is well stocked and should be utilized intelligently. The best defence is a good attack.

[1] N. Kopeloff: *Why Infections? In Teeth, Tonsils, and Other Organs.*

Chapter XXXII

CLASSIFICATION

The classification of microbes has been delayed as long as possible, not only because it is confusing and ever changing where it should be simple, but also because it is probably the most contentious of all bacteriologic subjects. Most classifications are based on the form (morphology) of microbes. But the whole gamut has been run, even down to a classification based on how microbes function (physiology). None of these criteria can be absolute, for the bacteriologist particularly well versed in any single group of microbes can always point to exceptions which defy arbitrary generalization.

When Koch first grew microbes on a solid media, he believed that certain properties were constant for any given bacterial species — namely, shape, motility, spore-formation, distribution of flagella, staining, colony-formation, and action upon sugars. To be sure, different species varied in these properties, but each species was stable. Any irregularities observed were ascribed to contamination or possibly degeneration. Above all, it was assumed that all bacteria reproduced asexually, by fission. Classification in Koch's day was, consequently, dogmatic.

But certain revolutionary conceptions are at the present time gaining ascendency. It is maintained that bacteria have a life cycle in which they pass through various stages, including a sexual phase. Much evidence for this has been adduced in this country by Löhnis and Mellon. Rods, for example, have been shown by them to produce granular or coccus forms. Equally disconcerting is the phenomenon known as "microbic dissociation," wherein a single species of bacteria may be separated by artificial means into two separate pure lines yielding rough and smooth colonies when grown on artificial media. After the recent brilliant contributions of Mellon and Hadley to this subject the intricate systems of classification which have long held sway threaten to collapse. Rods have been changed to

cocci, virulent cultures may be made harmless, and vice versa; motility, spore-formation, and fermentative and serologic powers can be definitely altered at will. In a word, the stability of bacterial species is vigorously assailed. Such changes are not mutations in the botanical sense in which de Vries used the term — they are even more fundamental.

The conceptions of a bacterial life-cycle and microbic dissociation are finding increasing favour. But the more conservative-minded bacteriologists, and they are undoubtedly in the majority, still cling to their time-honoured classifications. To the lay reader these classifications must necesarily appear involved. Still, they represent the common meeting-ground of most present-day bacteriologists and have a certain clarifying value.

The general relationship which exists between microbes may be presented thus in outline form (after Park and Williams):

Kingdom	*Subkingdom*	*Classes in which pathogenic species occur*	*Genera in which chief pathogenic species occur*
Plants (Moulds)	Moulds	Mycomycetes	Aspergillus, Penicillium
		Phycomycetes	Mucor
		Unclassified (*Fungi imperfecti*)	Microspora, Trichophyta, Sporotricha, Achoria, Coccidiodes
	Yeasts	Oidia Monilia Torula Saccharomyces	Oidium, Monilia, Torula, Saccharomyces
	Bacteria	Cocci (Coccaceæ)	Micrococcus, Diplococcus, Streptococcus, (Tetracoccus)
		Bacilli (Bacteriaceæ)	Bacillus (Bacterium)
		Spirilla (Spirillaceæ)	Spirillum (Spirochæta, Treponema)
		Higher bacteria (Trichobacteria)	Cladothrix, Nocardia (Streptothrix)

Kingdom	*Subkingdom*	*Classes in which pathogenic species occur*	*Genera in which chief pathogenic species occur*
Animals (Protozoa)	Flagellates	Flagellata	Cercomonas, Leptomonas, Herpetomonas, Trypanosoma, Leishmania, Trichomonas, Lamblia (Spirochæta, Treponema)
	Amœbæ (Sarcodina)	Rhizopoda	Entamœba
	Sporozoa	Telosporidia, Neosporidia	Eimeria, Hæmogregarinida, Proteosoma, Hæmamœba, Babesia, Rhinosporidium, Myxobolus, Nosema, Sarcocystis, etc.
	Ciliates	Ciliata	Balantidium

Unclassified: Ultramicroscopic organisms

E. B. Copeland has said: "The living things are not all plants or animals. Nature has been more resourceful, more thorough in trying out the possibilities. Another kingdom, that of the bacteria, using the word in an exact sense, is likewise world-wide in distribution, probably most numerous in individuals and very important in human relations." [1]

The bacteria, which have been our chief concern, are represented by the four classes:

1. Cocci — spheres
2. Bacilli — rods
3. Spirilla — spirals
4. Higher Bacteria — threads

These classes may be further subdivided. There are two principal classifications in vogue in this country. The first is that of Migula, which dates from before 1896; the second, that of a committee of the Society of American Bacteriologists, as published in Bergey's *Manual of Determinative Bacteriology* (1927). The main features of each of the above are as follows:

[1] *Science*, LXV (1927), 390.

MIGULA'S CLASSIFICATION (after Marshall)

ORDERS OF THE SCHIZOMYCETES

THIOBACTERIA — Cells contain sulphur. Colourless, or pigmented rose, violet-red by bacteriopurpurin — never green

EUBACTERIA — Cells free from sulphur and bacteriopurpurin, colourless or faintly coloured

FAMILIES AND GENERA OF THE EUBACTERIA

COCCACEÆ — Cells round in a free state, not elongating in any direction before division into 1, 2, or 3 planes

Cells without organs of locomotion

Streptococcus — Division in one plane
Micrococcus — Division in two planes
Sarcina — Division in three planes

Cells with organs of locomotion

Planococcus — Division in two planes
Planosarcina — Division in three planes

BACTERIACEÆ — Cells rod-shaped, longer or shorter, and only dividing in one plane, and elongating to twice the normal length before division

Cells straight, rod-shaped, without sheath, non-motile or motile by means of flagella

Bacterium — Cells without organs of locomotion

Cells with organs of locomotion

Bacillus — Flagella distributed over the whole body
Pseudomonas — Flagella polar

SPIRILLACEÆ — Cells spiral without sheath

Cells rigid, not snakelike or flexuous

Spirosoma — Cells without organs of locomotion

Cells with organs of locomotion

Microspira — With one, very rarely two or three polar flagella

Spirillum — Cells with polar flagella in tufts of five to twenty
Spirochæta — Cells flexuous
CHLAMYDOBACTERIACEÆ — Cells inclosed in a sheath

Cell-contents without granules of sulphur
Cell-threads unbranched

Chlamydothrix — Cell-division always only in one plane
Phragmidiothrix — Cell-division in three planes previous to conidia formation

Cells surrounded by a very delicate, scarcely visible, sheath (marine)

Crenothrix — Sheath clearly visible (in fresh water)
Sphærothrix — Cell-threads branched (pseudobranches)

FAMILIES AND GENERA OF THE THIOBACTERIA

BEGGIATOACEÆ — Filamentous bacteria which do not contain bacteriopurpurin. Cells contain sulphur granules
Thiothrix — Cells non-motile, threads attached to some object
Beggiatoa — Moves by means of an undulating membrane
RHODOBACTERIACEÆ — Cells contain bacteriopurpurin; sulphur granules may also be included. This family includes twelve genera as follows: Thiocystis, Thiocapsa, Thiosarcina, Lamprocystis, Thiopedia, Amœbobacter, Thiothece, Thiodictyon, Thiopolycoccus, Chromatium, Rhodochromatium, and Thiospirillum

THE FAMILIES AND GENERA OF THE BACTERIA

(Report of the Committee of the Society of American Bacteriologists)

ORDERS OF THE SCHIZOMYCETES

MYXOBACTERIALES — Cells united during the vegetative stage into a pseudoplasmodium
THIOBACTERIALES — Cells not forming a pseudoplasmodium. Cells free or united in elongated filaments, often with a well-defined sheath. Conidia frequently formed. Free sulphur, iron, or bacteriopurpurin often present

CHLAMYDOBACTERIALES — Sulphur and bacteriopurpurin absent; iron often present

EUBACTERIALES — Cells never in sheathed filaments. Conidia only in mycelial Mycobacteriaceæ. Flagella often present. Free iron, sulphur, or bacteriopurpurin never present

Families of the Eubacteriales

SPIRILLACEÆ — Cells spiral with polar flagella

COCCACEÆ — *Not as above*

Cells spherical; rarely if ever motile; spores never produced; never securing growth energy from nitrogen or ammonia

PSEUDOMONADACEÆ — *Not as above*

Cells short, rod-shaped, with a single polar flagellum, rarely two; usually forming green or yellow pigment

BACILLACEÆ — *Not wholly as above*

Spores formed

Spores never formed

NITROBACTERIACEÆ — Metabolism simple, securing growth energy from carbon, hydrogen, or their simple compounds; flagella, if present, polar

MYCOBACTERIACEÆ — Metabolism complex, dependent upon more complex carbohydrate and protein substances; flagella, if present, peritrichic. Cells clubbed, fusiform, filamentous, branching or mycelial; those not distinctly so are either acid-fast or show barred, irregular staining

LACTOBACILLACEÆ — *Not as above*

Gram-positive; non-motile

BACTERIACEÆ — Gram-negative; often motile

Genera of the Eubacteriales

I. NITROBACTERIACEÆ

Fixing nitrogen or oxidizing its compounds

Fixing free nitrogen

Azotobacter — Cells large: in soil

Rhizobium — Rods minute: in roots of leguminous plants

Oxidizing nitrogen compounds

Nitrosomonas — Oxidizing ammonia

Nitrobacter — Oxidizing nitrates

Not as above

Hydrogenomonas — Oxidizing hydrogen

Mycoderma — Oxidizing carbon compounds

Oxidizing alcohol; branching forms common

Not as above, using simpler carbon compounds

Carboxydomonas — Oxidizing CO

Methanomonas — Oxidizing CH_4

II. MYCOBACTERIACEÆ

Mycobacterium — Slender rods staining with difficulty and acid-fast

Not as above

Nocardia — Mycelium and conidia formed. With aerial hyphæ and conidia; usually saprophytic soil organisms

Actinomyces — Hyphæ and conidia not aerial; usually parasitic in animals

Not as above; cells rod-like, usually somewhat curved, clubbed, fusiform, or even branched, but never mycelial

Leptotrichia — Thick, long threads, fragmenting into short, thick rods

Not as above

Fusiformis — Cells usually elongated and fusiform; filaments, if formed, not branching; stains somewhat irregularly

Corynebacterium — Cells slightly curved, clubbed, or in old cultures even branching; not filamentous; showing definite barred staining

III. PSEUDOMONADACEÆ

Pseudomonas — Generic characters mainly those of family

IV. SPIRILLACEÆ

Vibrio — Flagellum single (rarely 2 or 3)

Spirillum — Flagella tufted (5 to 20)

V. COCCACEÆ

Rhodococcus — Abundant red-pigmented growth on agar

Not as above

Gram-negative

Neisseria — Normally in pairs of flattened cells; growth on plain agar scanty; never bright yellow

Normally in plates, packets, or irregular masses; growth on plain agar abundant; pigment definitely yellow

Sarcina — Cells in regular packets

Micrococcus — Cells not in regular packets

Gram-positive (exceptions rare and not easily confused with above genera)

Streptococcus — Cells normally in chains, sometimes in pairs (especially in acid environment), never in large irregular masses. Gelatin rarely liquefied. Growth on plain agar usually translucent, never heavy, never yellow or orange

Staphylococcus — Pigment orange (rarely lacking); gelatin often liquefied actively

Albococcus — Whitish to porcelain-white; liquefaction less vigorous

VI. BACTERIACEÆ

Erwinia — Plant pathogens

Not as above; saprophytes or in animal habitats (intestines, tissues, etc.)

Bacterium — Usually motile and exhibiting active fermentative powers; typically parasitic in intestines of man and higher animals; growing well on ordinary media

Not wholly as above

Hæmophilus — Growing only in presence of hæmoglobin, ascitic fluid, or serum

Pasteurella — Growth on media scanty, but less sensitive than the above; short rods with tendency to bipolar stain

VII. LACTOBACILLACEÆ

Lactobacillus — Generic characters mainly those of family

VIII. BACILLACEÆ

Bacillus — Aerobic, usually saprophytic; cells not greatly enlarged (if at all) at sporulation

Clostridium — Anaerobic, often saprophytic; cells frequently enlarged at sporulation

Chapter XXXIII

THE CONQUEST OF INFECTIOUS DISEASES

The conquest of infectious diseases is at once an achievement and a hope. It is an achievement in certain diseases, a hope in others. Bacteriology is now so readily taken for granted and medical science has so fittingly absorbed its contributions that we are likely to forget the status of infectious disease in the days before Pasteur and Koch. It is impossible, indeed, to estimate the number of human beings who have succumbed to infectious diseases throughout the centuries preceding the nineteenth. The historic epidemics alone are appalling. Literary as well as medical sources, from the Bible to Shakspere, attest the devastation wrought by epidemics of infectious disease. Noah Webster has chronicled them in *A Brief History of Epidemic and Pestilential Diseases*.

It is interesting to learn there that "pestilential disease attacked both man and beast in ancient Greece and Rome." The first plague in Rome occurred about the sixteenth year after its foundation. It has been said that this plague killed instantly without any previous sickness. This was 738 years before the Christian era. In A.D. 80, there were as many as *10,000 deaths from plague in a single day in Rome*, a city of about one million inhabitants. Reference has already been made to the "Black Death" of the fourteenth century, which ravaged Europe as well as Asia. What of the epidemics of succeeding centuries, not only of plague, but of cholera, influenza, typhoid fever, smallpox, yellow fever, etc.? Their toll in human life staggers the imagination. Armies fighting over the face of the earth were hotbeds of disease and left impoverished communities a resistless prey to virulent microbes. Emigration, the movement of small or large bodies of people, served to disseminate infectious disease. It seems a miracle that with all the mortality caused by disease humanity has not been wiped out of existence.

How can mankind fight the unknown foe? Preventive medicine is only now finding its place. As Descartes has said: "If ever the human race is raised to its highest practical level, intellectually, morally, and physically, the science of medicine will perform that service." Bacteriology, by which we really mean microbiology, in identifying the offending microbes paves the way for sanitation. Kill the microbe, eliminate the intermediate animal host (where there is one) and raise the standard of personal immunity — then infectious disease will be obliterated for all time. Progress in the eradication of infectious disease has been spectacular. Let us recapitulate the principal achievements in the light of what has been learned about microbes, what has been done to conquer them, and what remains to be done.[1]

One point which should be borne in mind throughout the outline to follow requires emphasis — namely, that the persistence of eradicable diseases is no criticism of bacteriology, but of the community which permits the existence of such a disease. Bacteriology can but point the way to prevention and eradication — an enlightened public must do the rest.

Diphtheria is the best example of the progress of medical science in conquering infectious disease. Even though the bacillus of diphtheria was discovered over forty years ago, practically nothing was accomplished in controlling the disease or alleviating its horrors until very recently. The parents of even twenty-five years ago lived in terror of the word "diphtheria," for it meant watching their dearest possessions, their children, succumb to an agonizing death. Today we not only know the bacillus which causes diphtheria, but can grow it artificially, test its virulence, inoculate animals, and, best of all, produce antitoxin. The Schick test establishes whether an individual is susceptible to or immune from the disease. If susceptible, antitoxin should be administered. Antitoxin is of inestimable value in the treatment of patients actually suffering from diphtheria as well as in the eradication of carriers of the disease. Statistics show conclusively that children who are properly Schick-tested and rendered immune by the administration of antitoxin do not contract the

[1] The interested reader will do well to consult *The Conquest of Disease* by T. B. Rice (Macmillan Co., 1927), which has been drawn upon freely for the present chapter.

disease, while those who through ignorance or fear fail to avail themselves of the discoveries of science succumb. Diphtheria has been conquered.

Scarlet fever has yielded in much the same manner as has diphtheria. The cause of scarlet fever is a blood-dissolving streptococ-

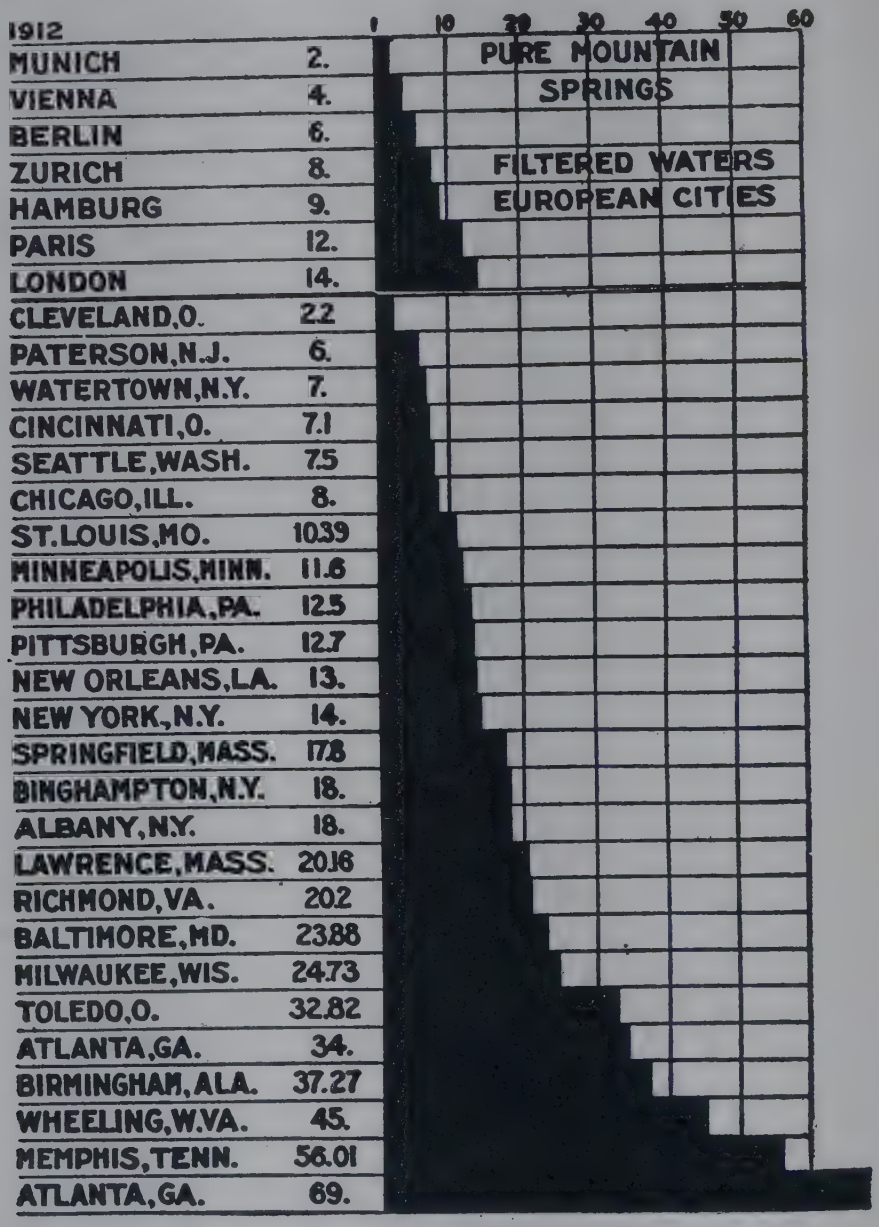


FIGURE 124

Average annual death-rate from typhoid fever in relation to water-supply. (After Marshall.)

cus. The Dicks have established a skin test for susceptibility which is analogous to the Schick test for diphtheria. Antitoxin renders the individual immune from the disease and is likewise of value in treatment. Further, it may be employed to yield a positive test for scarlet fever. The careful diagnostic routine examination of children's throats does much to prevent outbreaks.

Scarlet fever, therefore, is preventable. It is not only preventable but eradicable.

Typhoid fever is a filth disease. The typhoid-fever bacillus is to be found only in human excreta and objects which have come in contact with human fæces, urine, bath water, etc. To cause disease the typhoid-fever bacillus must enter the intestinal tract by the mouth. Apart from the dangers of typhoid infection it is difficult to understand how we can ever countenance the con-

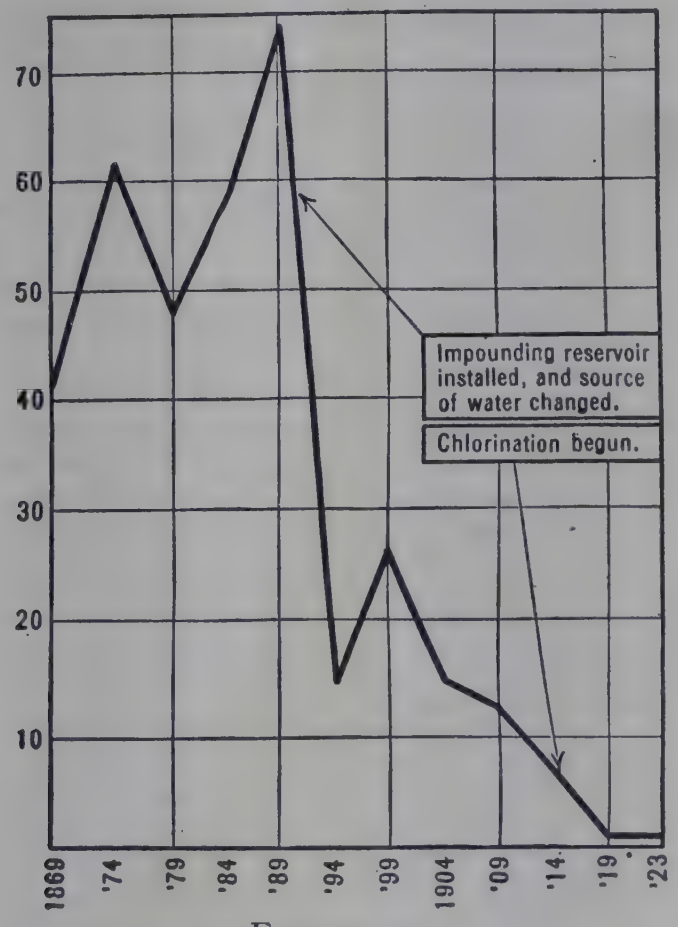


FIGURE 125

Typhoid-fever death-rate of Newark, N. J., in relation to its water-supply. (After Rice.)

tamination of our food and drink supplies. A pertinent question in every case of typhoid, says Rice, is "Whose excrement have you been eating, and when and where and why? . . . Control the means by which excrement can get into food or water or into people's mouths and there will be no more typhoid." The bacilli that cause typhoid and paratyphoid fever are well known. We can grow them and produce a vaccine. Vaccination renders the individual immune from the disease. Sanitary control of food, water, milk, and sewage, together with vaccination, spells the end of typhoid fever. (See figs. 124 and 125.)

Dysentery, like typhoid fever, flourishes in filth. The microbial cause is known. In India alone, it is estimated that 300,000 to 350,000 people die from the disease yearly. Vaccination, however, is still of doubtful value in dysentery. Prevention, therefore, depends chiefly upon sanitation.

Cholera, which has scourged the world with epidemics, has much in common with typhoid fever and dysentery. "Even as recently as 1902–1911 India suffered an epidemic of this disease which was responsible for the death of four million persons" (Rice). The causal microbe is different, but the conditions under which it causes disease are similar. Again, scrupulous sanitation and rigorous control of carriers are the bulwarks of prevention.

Smallpox represents the first triumph of vaccination. The horrors of smallpox in the eighteenth century are familiar. Almost everyone had the disease at some time or other. "It caused about one-tenth of all deaths, and about one-fourth of all mankind either died of it or was crippled or disfigured by it. During that century it was responsible for the deaths of about 60,000,000 persons in Europe alone. Thirty-six per cent of the population of Iceland died of the disease in a single year. Though Mexico in those days was far from being a populous country, 3,500,000 died there of smallpox in a few years" (Rice). Since the day when Jenner (1796) introduced vaccination against smallpox by the injection of cowpox virus, the incidence of smallpox has rapidly declined. We know little concerning the cause of smallpox save that it must be microbial because of the speedy manner in which it is transmitted. But we do know how the disease may be eradicated. The accompanying chart is proof positive. (See fig. 126.) The prevention of smallpox depends entirely upon vaccination and is not concerned primarily with sanitation, cleanliness, hygiene, or quarantine. "Vaccinated, you are safe; unvaccinated, you are a menace to yourself, your family, your friends and your community" (Rice).

Lockjaw or *tetanus*, which has claimed many more victims in times of war than in times of peace, has been successfully throttled by the use of antitoxin. Again, the bacillus has been identified, grown artificially, and used to produce antitoxin, which is more active in prevention than in treatment. The same

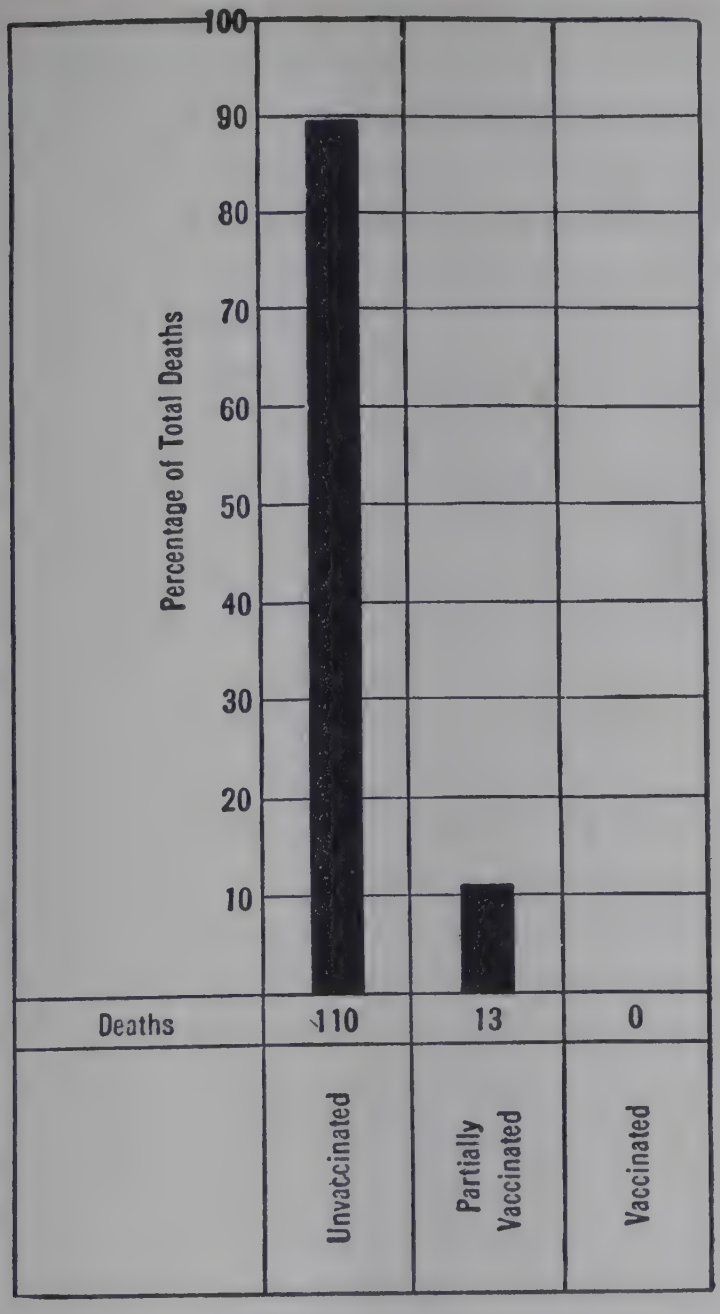


FIGURE 126

The value of vaccination in Denver, Colo.
(After Rice.)

may be said for the bacilli of malignant œdema and gas gangrene which are also intimately associated with war wounds.

Erysipelas, "St. Anthony's Fire," has long been the terror of hospitals. With the introduction of sanitary precautions the incidence of the disease has diminished. But the discovery of antitoxin has proved a still greater boon, for it may do much to rob erysipelas of its mortality and speed convalescence.

Botulism, and other food infections caused by the *enteritidis* group of bacilli, may be prevented by insistence upon clean food properly sterilized. The causal microbes have been described and

their power to produce toxins or poisons has earned for them considerable notoriety. Bacteriology has taught us how to handle food so that it may be just food and not a carrier of disease.

Avenues of infection cannot always be charted easily. Some of the diseases enumerated are transmitted by contact; some may be carried in the saliva or excrement; some are borne by insects; others choose more devious routes.

Hydrophobia or *rabies*, as everyone knows, is transmitted most often by the bite of an infected dog. Many a superstition has gained popularity concerning the treatment of this frightful disease. Celsus, a famous Roman medical writer of the first century, wrote: "The only remedy is to throw the patient unexpectedly into a pond, and if he has not a knowledge of swimming, to allow him to sink, in order that he may drink, to rise again, and again to depress him, so that, though unwilling, he may be satiated with water; for thus at the same time the thirst and the dread of water are removed. But another danger arises, lest the distention of the nerves may destroy the enfeebled body being harassed with cold water. Should this happen, the patient is to be taken immediately from the water and put in hot oil." A cheerful remedy!

Even more strenuous was another prescription to the effect that the wound inflicted by the rabid animal should be made larger, packed with gunpowder, and exploded. Other choice recommendations include the use of "mad stones" and special diets. Thanks to Pasteur, the bite of a rabid animal has been robbed of its terrors. But the prophylaxis which bears his name must be immediate to prove effective. Another means of prevention is to enforce the muzzling of dogs so as to reduce the possibility of attack. The Pasteur treatment is in use the world over. Its complete success as a preventive for rabies is another tribute to his genius.

Anthrax, *malta fever*, and *glanders* are essentially animal diseases which also attack man. But animals can be vaccinated against anthrax, just as man is vaccinated against diphtheria. In other words, stamp out the disease in animals, and man is secure. An added precaution in these days when animal products are so extensively utilized in the manufacture of furs and brushes is to require their sterilization prior to human use. In this way

FIGURE 127

Surgeon-General William C. Gorgas. (After Kelly.)

animal diseases will be confined to those comparatively few who look after animals.

Perhaps no simple group of infectious diseases has yielded more to sanitation than have the insect-borne diseases. Once bacteriology establishes the identity of the intermediate host, the rest is simple: exterminate the intermediate host. Thus have we conquered a group of diseases which have taken more lives throughout man's history than can be counted.

Yellow fever represents the outstanding conquest of American

medicine in the field of infectious disease. The tale has been told again and again from the days when Finlay, Reed, Carroll, Lazear, and Agramonte established that the *Stegomyia* mosquito, now known as *Aedes ægypti*, transmitted the disease, to the cleaning up of the Canal Zone by Gorgas (see figs. 127 and 128), and the discovery of the causal microbe by Noguchi. The finishing touches of prevention and treatment by the use of specific

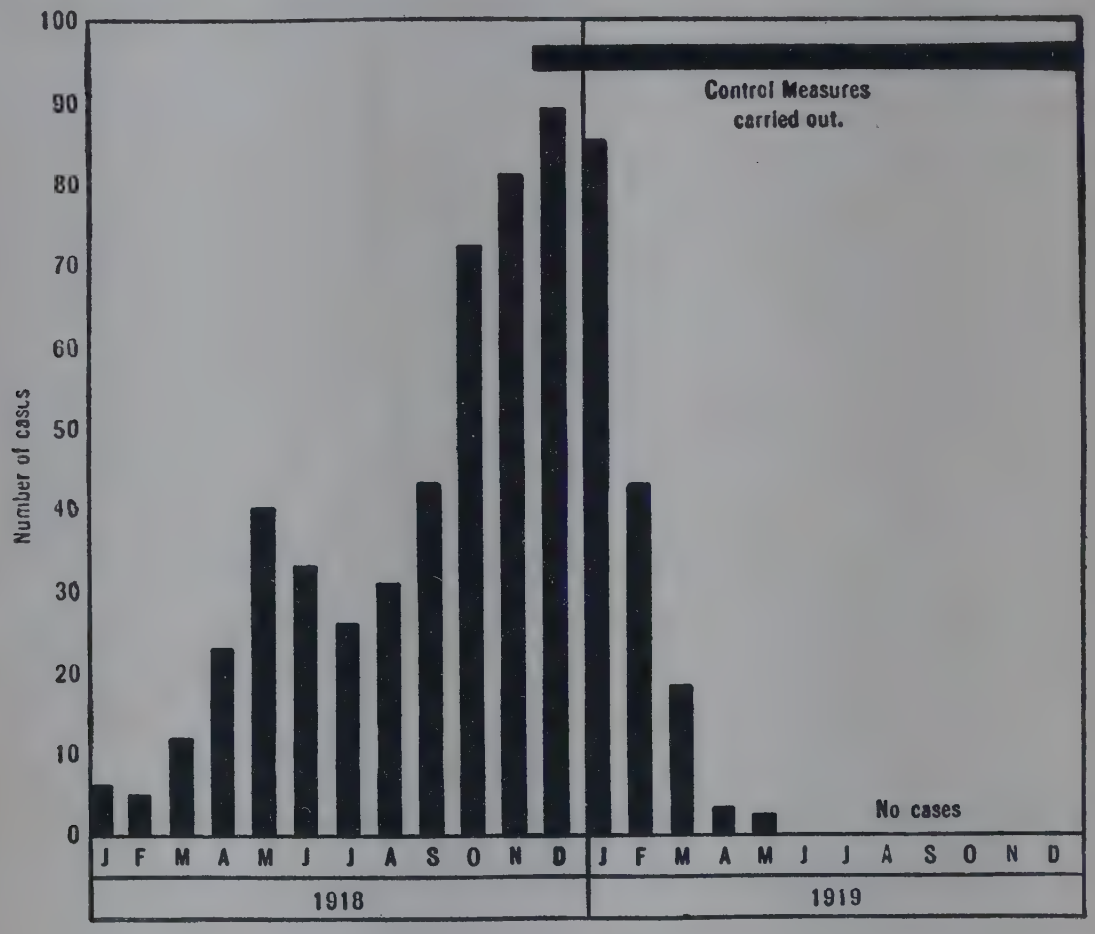


FIGURE 128

The eradication of yellow fever from Guayaquil, Ecuador.
(After Rice.)

serum made after the manner of diphtheria antitoxin await the final stamp of approval. Already many adherents have been gained. The fear of "Yellow Jack" has no more place in the hearts of men.

Malaria, which led to the downfall of "the glory that was Greece and the grandeur that was Rome" is another mosquito-borne disease. This time we indict the *Anopheles*. Its extermination is a difficult but not impossible task. Economically it may represent a tremendous undertaking — practically it will yield a handsome profit. The drainage of swamp-lands, the liberal use of

oil on stagnant water, the cultivation of fish and birds which prey on mosquitos, and the screening of dwellings have done much towards the eradication of malaria. Nor must we forget the use of quinine in treatment and prophylaxis, for it has a specific action upon malarial protozoa.

The French abandoned the project of the Panama Canal because of malaria, but Gorgas paved the way for Goethals to construct that gateway which now joins the Atlantic with the Pacific. The accompanying graph (see fig. 129), after Rice, shows the triumph clearly.

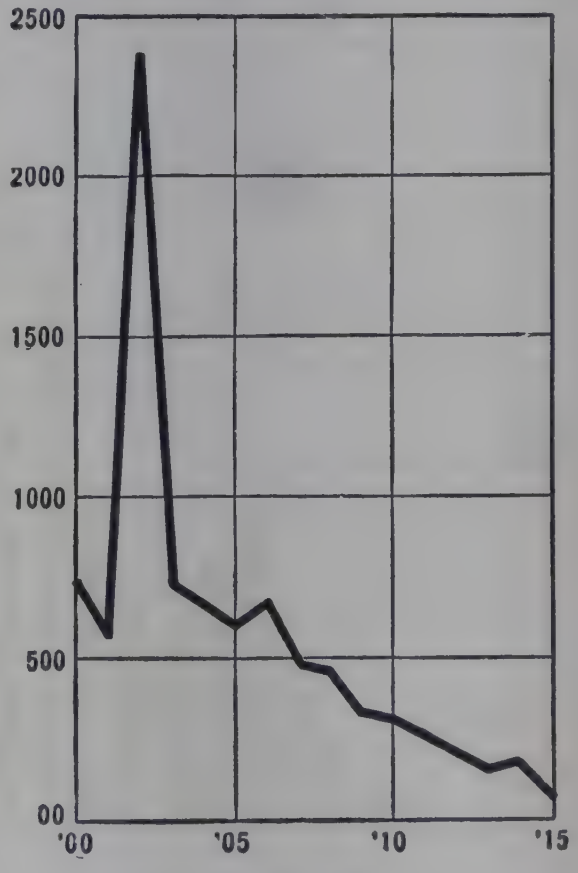


FIGURE 129

Malaria mortality-rate in Panama City. (After Rice.)

Plague, the "Black Death," requires little in the way of preamble concerning its destruction of human life in uncounted millions. *Bacillus pestis* is carried by fleas which infest the rat. "Swat the rat and you swat the flea; swat the flea and you swat the germ of plague" (Rice). The rat has been swatted. Rat-proofing of dwellings, warehouses, docks, and ships has made of plague only a memory in the United States. It can still be an epidemic disease where for one reason or another, chiefly economic or political, such precautions are not observed.

Typhus fever, like the other "pestilential diseases," thrives in filth because the lice which carry *Rickettsia prowazeki* are only to be found where people are unclean. Sanitation and personal hygiene have doomed the louse and with it typhus fever.

There is the romance of bacteriology and there is — romance. "In ye days of olde the brave knight fought horrible fire-spitting demons and dragons; he made crusades against the barbarians and Saracens; he rode forth to rescue fair maidens in distress. He sat proudly astride a fiery steed; his shiny armor glittered and flashed; he brandished his trusty sword and lance; and upon his

shield was emblazoned his coat of mail; he wore a lock of his lady's hair, forsooth. Warfare was a romantic adventure. Modern warfare against disease is quite prosy by comparison. The brave knight, and he needs to be brave, goes out to fight lice and fleas, and rats, and flies, and maggots and mosquitos, and filth and dirt. But he gets results that the knight of old never dreamed of" (Rice).

Sometimes the results are a long time coming. Nor are they all as gratifying or spectacular as the conquest of yellow fever, malaria, plague, and typhus fever.

The *common cold*, for example, has proved most evasive. Apparently a number of germs participate in the common cold. If there is any simple microbe chiefly at fault, it remains incognito. Recently the Chemical Foundation gave about two hundred thousand dollars to the Johns Hopkins University to further research in the study of the common cold. Being an infectious condition, it can be kept from spreading rapidly by preventing indiscriminate nose and throat discharge. Autogenous vaccines have proved successful in some instances, although they represent a haphazard approach to a difficult bacteriologic problem.

Influenza also eludes us. Different microbes have been identified as the cause of different epidemics, but little has been done in the way of prevention. Even the mode of transmission remains obscure.

Pneumonia, another respiratory infection, presents many difficulties. Bacteriologically progress has not been inconsiderable. We know the principal types of microbes capable of producing pneumonia. Serums and antibody solutions have been used with some success in treatment but there is little beyond common hygiene that is of avail as a preventive measure.

Whooping-cough offers a similar but somewhat more encouraging outlook. *Bacillus pertussis* is the offending microbe. Vaccines and convalescent-serum have been of value in ameliorating symptoms and it is claimed they have also served as a means of prevention. On the latter score alone, however, vaccines leave much to be desired.

Measles appears today to have the same status as that of scarlet fever a few years ago. In other words, it is believed that a

streptococcus is the cause of the disease. This finding, however, has not been universally accepted. Regardless of the specific cause, we have learned that by the use of convalescent-serum much can be done to lighten the attack and to avoid the serious complications which frequently ensue. Were the supply of serum from patients recovering from the disease not so limited, it could be used to advantage as a preventive. Indeed, convalescent-serum has been so used with conspicuous success.

Mumps belongs in the same category as measles, or perhaps a step below, for there is next to nothing known of the causal organism beyond the fact that it is ultramicroscopic in size. As in measles, convalescent-serum is said to have value both in treatment and prevention.

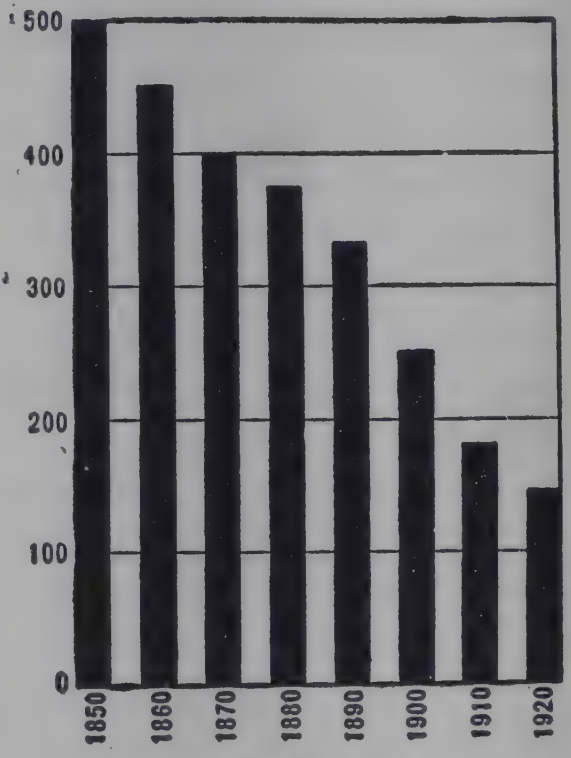


FIGURE 130

The decline of the tuberculosis death-rate in Massachusetts. (After Rice.)

Tuberculosis, the "Captain of the Men of Death," yields steadily but surely to advancing civilization. Bacteriologically some progress has been made, notably in the identification and culturing of *Bacillus tuberculosis*. But the improvement in sociologic and hygienic conditions and the general care of infants has probably been the most important factor in lowering the mortality and incidence of this disease. The accompanying chart gives point to such a statement. (See fig. 130.) Medicine has undoubtedly done its share, as have the various public health agencies. The prevention of this disease is an ideal worthy of realization. When the cause has gained enough adherents, tuberculosis will have been robbed of its terrors.

Infantile paralysis, *sleeping-sickness* (*lethargic encephalitis*), and *spinal meningitis* are among the most difficult infectious diseases to control. Only in spinal meningitis do we know the causal microbe — the meningococcus. In all of these three diseases infection probably occurs through the respiratory tract, chiefly

the nasopharynx. Specific serums have been used in treatment, but only in infantile paralysis have they been promising. Little can be done in the way of prevention beyond isolation.

Having considered the infectious diseases which have yielded to man's control and those in which some progress has been made, there remains still another interesting group in which the causal microbes have been identified, yet in which the treatment and prevention is not by vaccines, antitoxins, or serums, but by drugs.

Syphilis, often called the "Fourth Plague," began as an epidemic disease of great virulence and mortality and has ended by becoming thoroughly socialized. The spirochæte that causes syphilis has not only been seen under the microscope, but been grown artificially. No vaccine, antitoxin, or serum, however, has as yet been successfully prepared. Thanks to Ehrlich, arsenic-bearing compounds, notably arsphenamine (salvarsan) and neo-arsphenamine (neo-salvarsan), have proved specific in the treatment of the disease. To these must now be added tryparsamide, developed by Jacobs and Heidelberger. Mercury and iodides also have value in treatment. Furthermore, mercury is of particular importance in prophylaxis. In general paralysis (the final stage of syphilis) malarial therapy, introduced by Wagner von Jauregg, has won world-wide recognition. Syphilis, serious as it is to the patient and to society, has fallen under the domination of medical science. The way to treatment and prevention is clear. Enlightenment and public policy can eradicate the disease.

Gonorrhœa, the twin of syphilis, is regarded by some authorities to be woman's greatest single cause of misery. It has been said that there is probably no other disease known to medical science which has caused so much suffering and sorrow in the civilized world as gonorrhœa, for it has been estimated that this disease is responsible for sixty-five to seventy-five per cent of all pelvic operations upon women and fifty to eighty per cent of all sterility. About ten to thirty per cent of all blindness is due to gonorrhœal inflammation of the mucous membrane of the eyes of new-born children. The illness, inefficiency, and expense caused annually by the two venereal diseases, gonorrhœa and syphilis, has been computed at three billion dollars. The treatment of gonorrhœa in the hands of competent members of the medical

profession, and not of quacks, has done much to reduce the dangers of this disease. From the standpoint of public health, prevention is of even greater importance. Prophylaxis, consisting of injections into the urethra of protargol, etc. *immediately* after exposure to infection has materially reduced the incidence of gonorrhœa, as proved by recent army experience. Since traditional morality has proved ineffective in dealing with irregular sex relations, the responsibility of the individual in the interests of social hygiene requires that at least prophylactic measures be employed. The value of injecting silver-nitrate solution into the mucous membranes of the eyes of the new-born to prevent blindness is well established. Gonorrhœa is a preventable disease. Society has all the facts necessary to eradicate it. Medical science has done its share — the public must do the rest.

Leprosy is a disease that has terrorized mankind since antiquity. It has claimed many voluntary martyrs among its victims. We know the bacillus that causes leprosy, but little more. Segregation is the traditional precaution, which, of course, must be observed to prevent further spread of the disease. The most promising therapeutic agent in the treatment of leprosy, which is rapidly gaining popularity, is chaulmoogra oil. Progress, therefore, has been made in leprosy.

Drugs have also been used to advantage in other infectious diseases:

Vincent's angina or *trench mouth* yields to arsphenamine (salvarsan) applied locally in the throat or injected into the veins, or to sodium perborate used as a mouth-wash. All three methods together are very effective in curing the disease.

Yaws, the tropical disease which is practically indistinguishable from syphilis, is also successfully treated with arsphenamine (salvarsan).

African sleeping-sickness has been effectively treated by "Bayer 205" and atoxyl.

In this brief account of the conquest of infectious diseases the attempt has been made to indicate the nature of the principal diseases that have beset mankind; the rôle which bacteriology has played in the identification of the causal agents; the development of methods for treatment and prevention of the diseases under consideration; and, finally, the part which drugs have

played pending the perfection of suitable bacteriologic procedures. The contributions of bacteriology, or, better still, microbiology, to medical science have become so integrated that they threaten to lose their identity. It has been the purpose of the present volume, therefore, to detail these contributions, together with others of an agricultural or industrial character.

Man *versus* Microbes! Through the microscope we have followed the conflict, in which man has gained many a signal victory. The struggle has endured since man first made his appearance upon this planet and it will endure until his adversaries are entirely within his power. To such an end bacteriology is consecrated.

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